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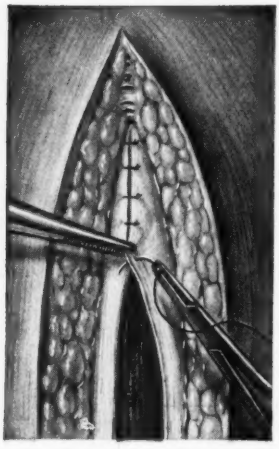

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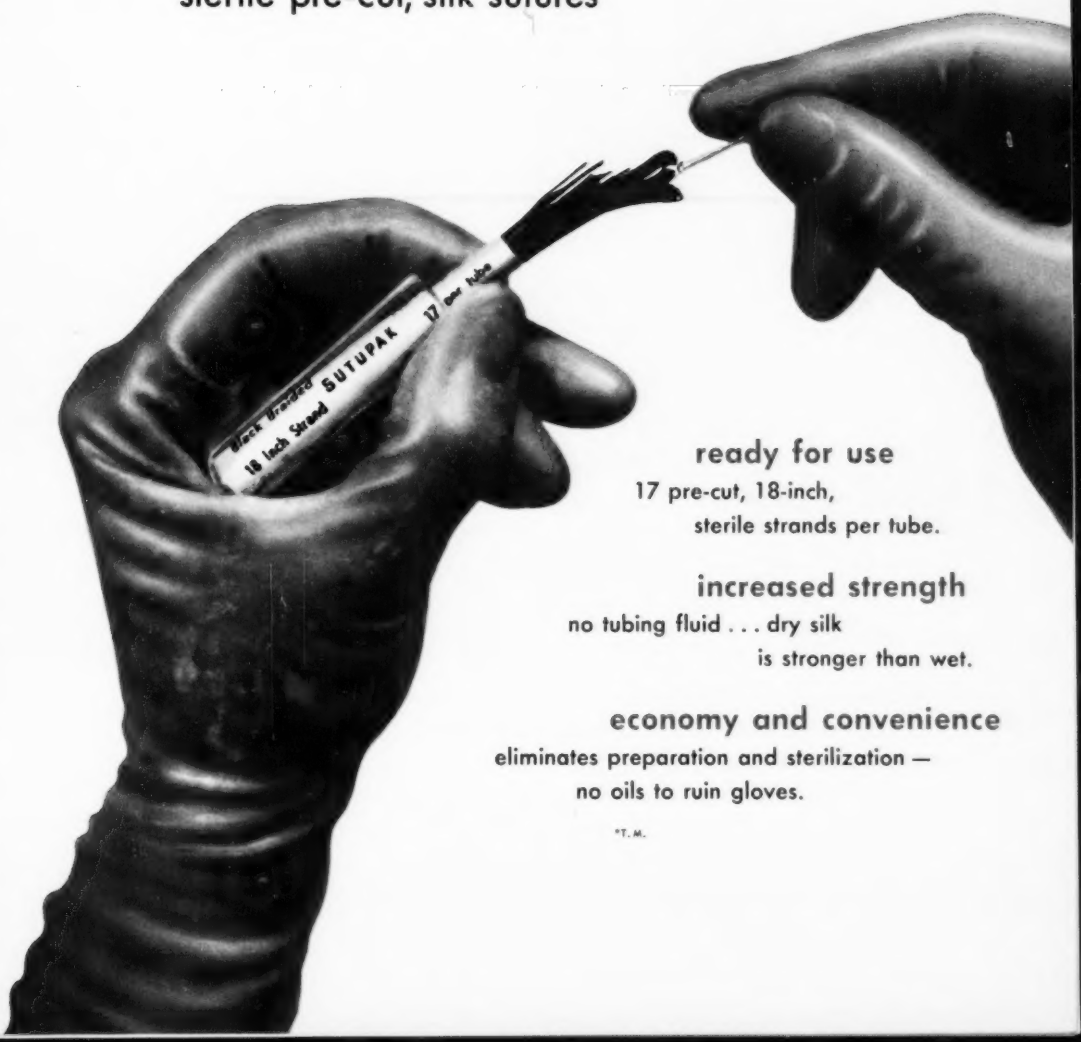

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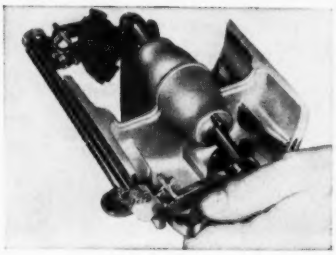

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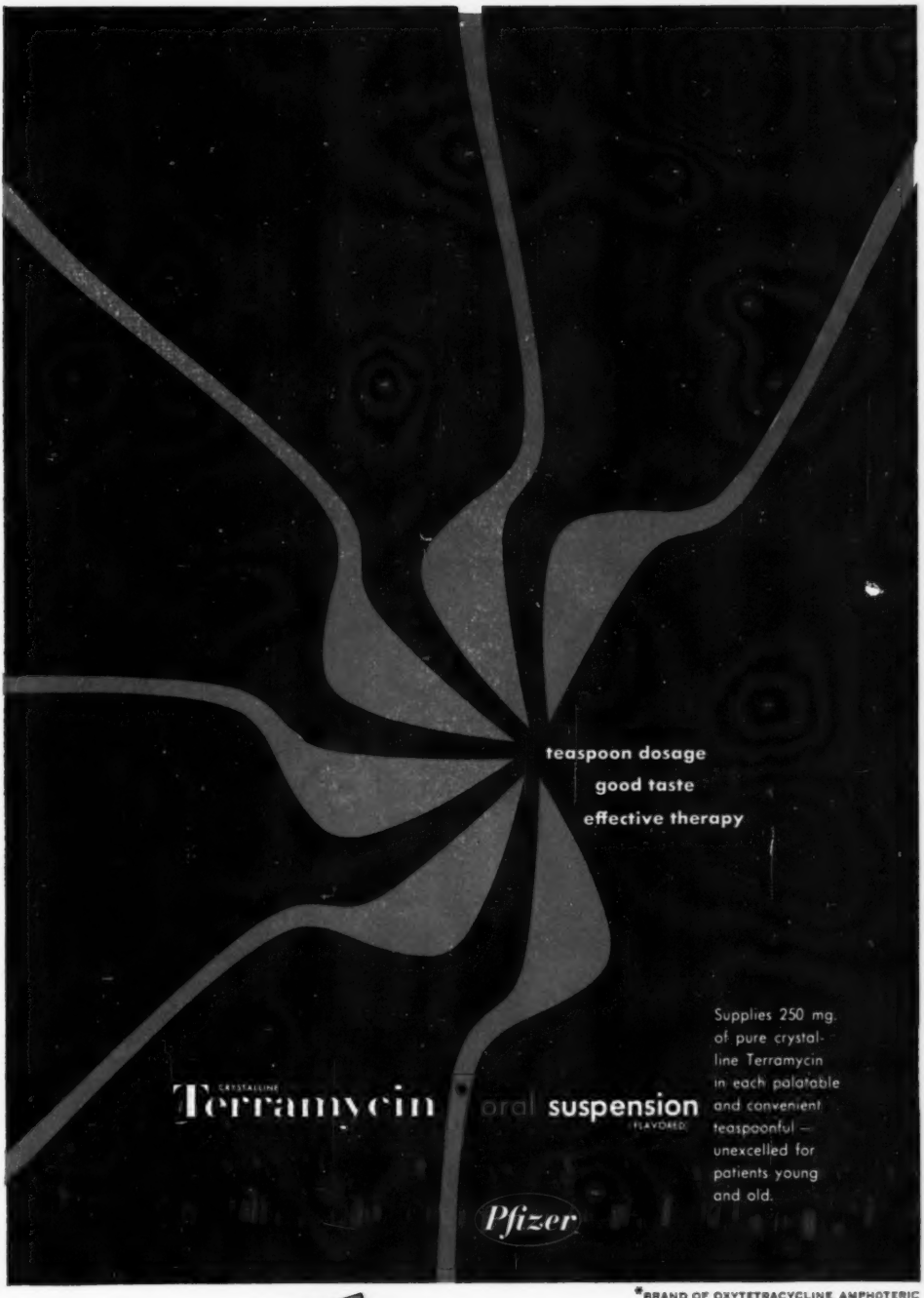

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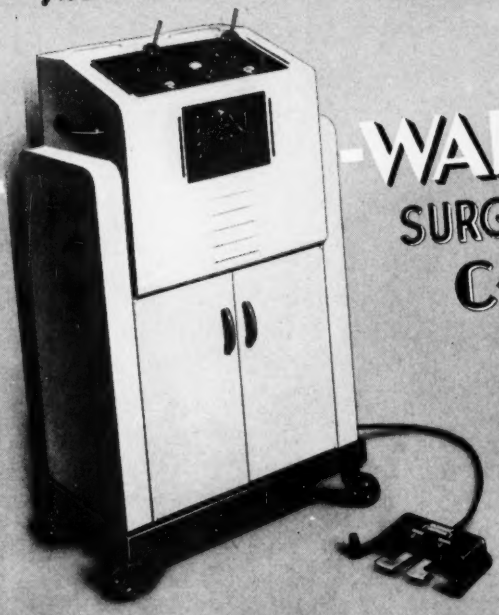

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VOLUME 66 FEBRUARY 1953 NUMBER 2

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ARTIFICIAL VAGINA

Preliminary Report of a New Combined, Anatomic, Mechanical, and Endocrine Approach

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THE SURGICAL creation of an artificial vagina still intrigues the medical profession. In the past 135 years, countless and tedious methods have been devised only to be discarded because of the magnitude of the procedure and/or the inability to cope with the serious complications.

Dupuytren in 1817, Villaume in 1829, and Amussat in 1832,[1] made a simple opening between the bladder and rectum but could not satisfactorily maintain its caliber. Eventually, methods and materials for lining the pouch were outlined. Free skin flaps, strips of vaginal mucosa from other patients, intestinal wall from both the small and large bowel, hernial sac lining, guinea-pig intestine, peritoneum, fetal membranes, and, lately, Thiersch grafts have been utilized. Heppner, Gersung, Baldwin, Schubert, Graves, Wharton, Falls, Counsellor, and Frank contributed techniques to this end.

While all these methods were initiated by the dissection of the area between the bladder and rectum, their greatest differences were marked by the manner in which the space was lined and its patency maintained. Today these are still the greatest drawbacks, although recent efforts appear to have minimized greatly these factors.

CONTEMPORARY METHODS OF SURGERY

It is interesting to note that despite the ever-increasing technical ability of the surgeon the evolution of this operation has been toward simplification. The monumental work of Robert Meyer [2] provides the basic principle for most of the contemporary methods of surgery. He demonstrated that the

vagina is formed by the fusion of the epithelium of the urogenital sinus and the Mullerian systems; that the Mullerian segment is encroached upon by the progressive invasion of the sinus; that ultimately all the epithelium of the Mullerian canals is replaced by the invading epithelium of the Sinus Urogenitalis.

From the Gynecological Divisions of Cook County Hospital, Chicago Medical School, Cook County Graduate School, and Grant Hospital.

1. Whitacre, F. E., and Chen, C. Y.: Am. J. Obst. & Gynec. **49**:789, 1945.
2. Meyer, R.: Arch. Gynäk. **158**:639, 1934; **163**:205, 1936; **164**:207, 1937; **165**:504, 1938; **166**:306, 1938.

That the invasive potential is still retained, even though its embryological development may be thwarted, is demonstrated by a series of cases reported separately by Wharton and Counsellor.

Wharton introduced his technique in 1938,[3] basing it primarily around the insertion of a solid vaginal mold into the dissected space to maintain patency and allow the squamous epithelium of the introitus to proliferate and spread to cover the walls of the newly created vaginal space. A balsa-wood form covered with two thicknesses of rubber condom was placed into a widely and deeply dissected vaginal space and retained for three weeks. Subsequently, it could be removed for sanitary purposes at frequent intervals over a period of three months, at which time the vaginal tract was covered by a layer of pale thick epithelium.

Recently Wharton and others have been using Thiersch grafts taken from the thigh and sewed over the form, which is then inserted into place. Usually the graft takes well in several weeks, but the form must be kept in place until the healing is firm. A prodigious series was reported by Counsellor in 1948,[4] covering 76 cases of congenital absence of the vagina and its surgical treatment. Of the total, in 70 cases treatment was by utilization of Thiersch grafts, and in 6 cases management was by simple dissection and insertion of the mold alone. As with others who performed this type of procedure, Counsellor recognized that if the factor of contraction is disregarded, there is bound to be a poor result or failure. It was McIndoe [5] who pointed out that the contraction factor of any canal may last three to six months or longer and that if the vaginal form is removed before the "contraction" disappears stricture will result. Success or failure in Counsellor's series inevitably seemed to follow the length of time the patient "followed instructions" concerning the wearing of the vaginal mold.

In his report, in 55 of the 70 cases with grafts the results were excellent although in two secondary grafting procedures were done; in 10 the results were fair because of incomplete epithelization and slight contractures, yet in 7 cases the patients were able to maintain satisfactory sexual relations; in 5 cases the results were poor, or failure occurred subsequent to infection, or the graft did not take. Eventually, marked stenosis appeared in the latter cases.

Most significant was the fact that in all 6 cases with no graft the results were excellent. The vaginas completely epithelized, there were no contractures, and no additional surgery was necessary. He produced a vagina completely lined and normal in depth, diameter, and mobility. As long as six months of treatment was often necessary to attain this end.

Falls [6] describes a method which bypasses the prolonged intubation period necessary to overcome contraction and is of special value in those patients in whom a vaginal vestibule is already present. A small disc of skin is fashioned over the proper vaginal location. After the loose connective tissue between the bladder and rectum has been separated, this disc of skin is pushed inward to form the vault of the new vagina. Additional skin flaps are created from the lateral vulvae walls and sewed to the disc, allowing epithelization to occur between the transplanted strips.

3. Wharton, L. R.: Ann. Surg. **107**:842, 1938.
4. Counseller, V. S.: J. A. M. A. **136**:861, 1948.
5. McIndoe, A. H., and Banister, J. B.: J. Obst. & Gynaec. Brit. Emp. **45**:490, 1938.
6. Falls, F.: Am. J. Obst. & Gynec. **40**:906, 1940.

TeLinde [7] modified this method by allowing the disc to form part of the posterior wall and dissecting past it up to the peritoneum to create a deeper vagina. The disc here served as an epithelial island from which epithelization of the deeper part of the vagina took place.

PRINCIPLES OF PROCEDURES

Certain fundamental concepts have been gathered from a sufficiently large number of operations for congenital absence of the vagina, and it would appear that all subsequent procedures should embody these principles.

1. The ability of the vaginal canal to epithelize by itself is of extreme significance. It may not be necessary to resort to a grafting if care is taken to insure an adequate period of treatment. Dissection alone is a simple method and involves little risk.

2. The principle of mechanical prevention of contraction by means of an inserted mold is a must for a successful result.

3. Vaginal, perivaginal, and perirectal inflammation must be prevented, since this is the most important factor in scarring, shortening, and contraction of the new tract.

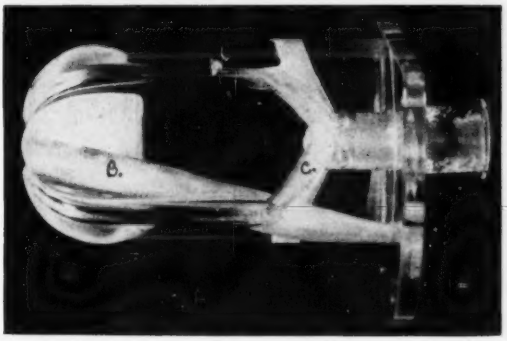

Fig. 1.—Lateral view of vaginal plug with integrated irrigating system (twice normal size).

COMMENT

1. *Additional Concepts.*—It is the purpose of this report to present additional concepts gathered from recent experiences with the procedure and to describe a method which encompasses the aforementioned fundamentals. The uniformly good results obtained in seven cases stimulated us to submit a preliminary report. Our past experience with Wharton's technique has been satisfactory, however; in certain cases our greatest obstacle seemed to be the presence of infection and our inability to combat it. We came to feel that if the dissected space could be frequently and adequately irrigated and drained without removing the insert, this obstacle could be overcome. To accomplish this, a simple plastic plug was devised (Fig. 1). This plug is constructed of lucite® and is shaped like a penis. It is rigid enough to resist the constant pressure of the powerful perineal muscles; it is smooth, so that it will not adhere to the side of the vagina; clean and easily sterilizable; nonabsorbent; it is light, so that it does not cause undue pressure on the bladder and rectum, and it is so fashioned as to provide a simple but adequate inflow-outflow irrigation system (Figs. 1 and 2). We are now able to irrigate the new space with a bactericidal solu-

7. TeLinde, R. W.: Operative Gynecology, Philadelphia, J. B. Lippincott Company, 1946.

tion thereby reducing the incidence of postoperative infection. This device is sewed into place to prevent any slipping, and thus the patient is permitted to be out of bed within a relatively short period of time following surgery.

2. *Postoperative Dilation.*—Almost a century ago the practice of forming a useful vagina by means of daily pressure against the vaginal space was advocated. In 1935 this practice was revived by Frank,[8] and, with perseverance, he was able to create a satisfactory tract when the tissues would yield. Wharton modified this concept by inserting a molded form into the dissected space and retaining it for long periods of time to prevent the tract from narrowing. We feel that this method, though satisfactory, unduly taxes a patient's cooperation, and, while it does aid in preventing contractures, it provides no allowance for lengthening the canal, a point which we feel should be stressed.

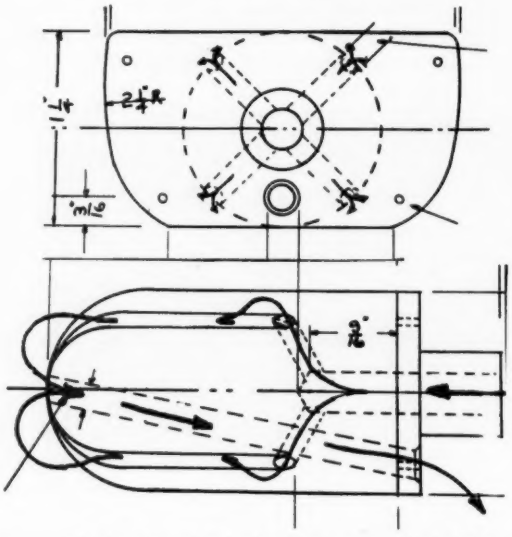

Fig. 2.—Diagrammatic drawing of irrigation scheme contained within vaginal plug. Arrows (lateral view) trace course taken by irrigating fluid. Injected through center bore, communication is made with exterior of form via four-pronged spider. Outer surface is grooved to allow fluid to flow toward tip and bathe entire surface simultaneously. Excess fluid is drained through wide slanted bore and captured in bedpan. Wide flange has been leveled off above and below to avoid contact with urethra and rectum.

The normal vagina is a distensible tube, larger in the marital state than in the virgin, and larger in the multipara than in the nullipara. This condition is primarily due to the dilatory effects of intercourse and childbirth. We have adopted this fundamental procedure by utilizing simple plastic forms for protracted postoperative dilation (Fig. 3).

These dilators are likewise made of lucite,® shaped like a penis, and graduated in length and circumference. A strong lucite® handle enables the patient to manipulate them easily. This handle can be securely fastened to any form over a threaded nipple. Self-dilation for 10-minute periods, several times a day, is easily carried out

8. Frank, R. T.: Am. J. Obst. & Gynec. **35**:1053, 1938.

and is sufficiently adequate to accomplish its purpose. On the patient's retiring, the dilator can be left in place and so held by an ordinary sanitary napkin, which has been perforated by the nipple of the dilator. Subsequent changes in the size of the dilator gradually enlarge the depth and diameter of the new orifice.

3. *Estrogen Stimulation.*—It is a well-known fact that estrogen will promote thickening and cornification of the vaginal walls. Moreover, it apparently increases the vascularity around the genitalia, as is evidenced by the production of estrus in test animals.[9] These factors are of paramount importance. It has been our experience that when estrogenic substances are administered systemically and locally they will materially facilitate and expedite the rate of epithelization in the artificial canal. We have been using a water-soluble estrogenic cream [10] as a lubricant for the postoperative dilators, as well as for initial use on the vaginal mold at the time of surgery. This provides the patient with a daily substantial amount of local estrogenic effect. In addition, we employ oral estrogen, with gradual tapering in the amount as permanently satisfactory results are obtained.

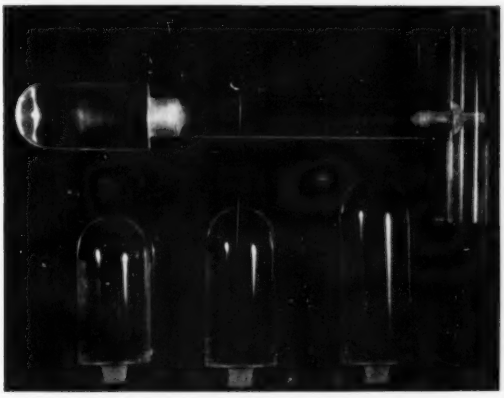

Fig. 3.—Lucite® forms for postoperative self-dilation. Handle is interchangable, fitting to any size form. Vaginal forms are graduated in length (2¼ to 2½ to 2¾ to 3 in. [5.7 to 6.3 to 6.9 to 7.6 cm.]) and in diameter (1¼ to 1½ in. [3.1 to 3.8 cm.]).

SURGICAL TECHNIQUE

The surgical technique employed suggests a modification of the procedure outlined by Wharton. In separate stages, an inverted T-shaped incision is made, the vertical limb actually representing a deep perineotomy. This additional step provides a larger orifice to the vagina and is a significant factor in diminishing the degree of contraction that ordinarily follows.

1. The usual preoperative routine is carried out, and the patient is placed in an exaggerated lithotomy position. The labia are placed on a stretch and sutured back, thus exposing the locale of the vaginal vestibule.

2. A metal catheter (No. 16) is inserted into the urethra and bladder to its fullest extent and the bladder emptied. The catheter is kept in place to mark the farthest point to which future dissection will be carried.

9. Goldzieher, M. A.: J. Gerontol. **1**:196, 1946.

10. Premarin® was supplied by Ayerst, McKenna, & Harrison, Ltd., New York 16.

3. At the lower pole of the rudimentary vestibule, tags of skin are picked up by Allis forceps, approximately 1½ to 2 in. (3.8 to 5.0 cm.) apart and placed on a stretch. A small segment of skin between the two forceps is excised, thus forming the initial horizontal segment of the T-shaped incision (Fig. 4*A*).

4. By sharp and blunt dissection of the loose areolar tissue, the new vaginal tract is created, advancing inward as far as the point of the metal catheter (Fig. 4*B*). Care is taken to main-

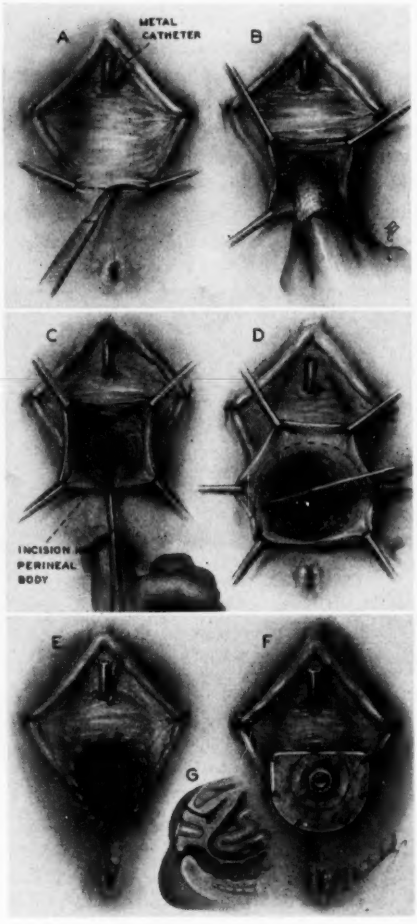

Fig. 4.—Surgical technique: *A*, small segment of skin between forceps is excised; thus forming initial horizontal segment of T-shaped incision; *B*, new vaginal tract is created, advancing inward as far as point of metal catheter; *C*, with finger in rectum, vertical incision is made with scalpel; *D*, excess mucosal tissue is excised; *E*, continuous whip stitch is used to anchor skin edges without incorporating muscle; *F* and *G*, lucite® plug is placed firmly into dissected space, its position being maintained by sutures through holes provided for it in wide flange of plug.

tain the same width as the original incision. A finger in the rectum will similarly aid in guiding the length of dissection. The vertical limb of the incision is now ready to be made.

5. With the finger in the rectum, a vertical incision is made with a scalpel, beginning at the junction of the lower and midthird of the new vaginal opening and is carried downward and forward through the perineal body to the external anal sphincter (Fig. 4*C*). (This incision

cuts through the lower border of the urogenital diaphragm thereby releasing the deep transversus perinei, the posterior limb of the bulbocavernosus, and superficial transversus perinei muscles, plus the decussating levator fibers of Luschka which are simultaneously separated. Except for the latter fibers, all are derived from the primitive cloacal sphincter.) This step greatly increases the diameter of the new orifice and releases much tension throughout the length of the vaginal canal, especially in the perineal portion. The posterior wall of the vaginal space will sag and some of the constricting potential of the surrounding muscles is lost.

6. The perineal portion of the vertical limb is then retracted on both sides and the exposed fascia freed from its underlying muscle allowing the latter to retract. The excess mucosal

Fig. 5.—Photomicrograph of biopsy specimen taken from apex of artificial vagina four months after surgery. Squamous epithelium is many-layered and well cornified.

tissue is excised (Fig. 4*D*), and a continuous whip stitch is then used to anchor the skin edges without incorporating the muscle (Fig. 4*E*). This step further increases the vaginal opening and provides hemostasis.

7. The lucite® vaginal plug is then generously coated with a water-soluble estrogenic vaginal cream and placed firmly into the dissected space. Its position is maintained by suturing it into place with nonabsorbable surgical (silk) sutures through the holes provided for it in the wide flange of the plug (Fig. 4*F* and *G*).

8. A Foley catheter is placed in the bladder.

Postoperative Management.—As soon as the patient can tolerate oral medication, 2.5 mg. of a natural-occurring conjugated estrogen is prescribed for intake three times daily. An intramuscular injection of penicillin, 600,000 units, is given immediately postoperatively and

continued daily for about 10 days. Irrigation of the operative site is facilitated by the system contained within the plug. A solution of bacitracin (200 units per cubic centimeter) is injected into the vagina through the center bore, the outflow being caught in a basin placed under the lower hole in the plug. This irrigation is done three times daily.

On the fourth postoperative day the Foley catheter is removed and the patient allowed to be out of bed, the vaginal plug being still in place. We have found that by the 10th day, if no fever is present, the operative site has healed sufficiently to allow the patient to go home. The vaginal plug is removed 10 days later, or approximately three weeks after its insertion.

All medication except the oral estrogen is now discontinued. At this time the patient initiates self-dilation of the vagina with the plastic dilators provided for her. Beginning with the smallest size dilator, daily periods of dilation for 10 minutes each, three times a day, are carried out. We prescribe again the estrogenic vaginal cream both for its lubricating effect when placed on the dilator and for its local specific action. In about three weeks, sufficient dilation has been afforded to allow the patient to use the next size dilator, and this increment of graduation is continued until the largest size dilator is used. After an additional three weeks' dilation with this dilator, using the estrogenic cream, the periods of dilation are gradually reduced until eventually three or four times a week is sufficient. In addition, the oral doses of estrogen are likewise scaled down until there is no further need for the drug.

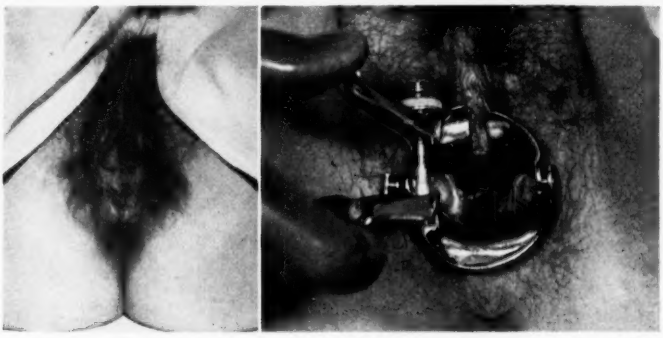

Fig. 6.—Right, postsurgical photograph. Speculum in place reveals acquired depth and roominess. Left, preoperative photograph showing well-developed external genitalia.

At four months these patients should have a completely healed vagina which admits a full-sized vaginal speculum and is lined with abundant squamous epithelium (Fig. 5), permitting adequate sexual satisfaction without dyspareunia (Fig. 6). Subsequent dilation depends on the frequency of coitus, with a minimum of the latter and additional dilation to total three times a week for a year.

SUMMARY

The management of congenital absence of the vagina is discussed. A method embracing the use of (*a*) a simple plastic vaginal form with a built-in irrigating system, (*b*) complementary use of oral and local estrogenic substances to expedite healing and vaginal epithelization, and (*c*) prolonged postoperative self-dilation with graduated plastic dilators, is outlined.

The surgical technique is described in detail. The important step in this procedure is the vertical incision through the perineal body. This provides a larger orifice through the vaginal space and appears to be a significant factor in diminishing contraction.

Dr. Sol Sugar cooperated in this study by permitting the inclusion of one of his cases in this series.

Mr. Elmer Mills made suggestions in the development of the mechanical plug and the dilators.

BLOOD TRANSFUSIONS IN HEMORRHAGE FROM A SEVERED ARTERY

Experimental Study

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THE TREATMENT for severe hemorrhage from peptic ulcer is still a controversial subject. There are those such as Stewart and his colleagues,[1] who advocate prompt operation in all cases; there are others, such as Dunphy and Hoerr,[2] who determine whether or not emergency operation is indicated by the initial response of the bleeding patient to conservative therapy, and finally, there are those, such as Andresen,[3] whose treatment in all cases is by medical measures. A discussion of the relative merits of these three schools of thought is beyond the scope of this paper. There remains a further difference of opinion as regards the use of blood transfusion in the presence of active bleeding from ulcer. Numerous ideas have been recorded regarding the indications for transfusion, the speed of administration, and the amount of blood which should be given.

The opinion of one group is exemplified by the following statement of Sandusky and Mayo:[4] "Complete and prompt replacement of the blood lost by hemorrhage must be accomplished and efforts in this direction must not be relaxed until the bleeding is brought under control and the blood volume restored to normal." Likewise, to quote Allen and Benedict,[5] "We have seen patients die from lack of blood, but in no instance have we seen transfusions responsible for fatal hemorrhage." On the other hand, there are many authors who feel that transfusion should be used sparingly in the presence of active bleeding. According to Andresen,[3] "Transfusions of 500 cc. or more often tend to aggravate the hemorrhage and may result in death." Bockus[6] reserves blood transfusions in cases of hemorrhage for those in shock or with a red cell count below 2,000,000, because of the fear that increasing the blood

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1. Stewart, J. D.; Rudman, I.; Citret, C., and Hale, A. W.: The Definitive Treatment of Bleeding Peptic Ulcer, Ann. Surg. **132**:681-689, 1950.

2. Dunphy, J. E., and Hoerr, S. O.: The Indication for Emergency Operation in Severe Hemorrhage from Gastric or Duodenal Ulcers, Surgery **24**:231-238, 1948.

3. Andresen, A. F. R.: Management of Gastric Hemorrhage, New York J. Med. **48**:603-606, 1948.

4. Sandusky, W. R., and Mayo, H. W., Jr.: The Management of Severe Bleeding from Gastric, Duodenal and Jejunal Ulcers, South. Surgeon **15**:69-82, 1949.

5. Allen, A. V., and Benedict, E. B.: Acute Massive Hemorrhage from Duodenal Ulcer, Ann. Surg. **98**:736-749, 1933.

6. Bockus, H. L.: Gastroenterology, Philadelphia, W. B. Saunders Company, 1945, Vol. 1.

volume might prolong bleeding. Bowers [7] states: "It is preferable that the blood pressure remain at a level slightly below normal so that clotting may more readily occur."

It would seem that the idea of replacing lost blood volume is on a more rational and firmer physiologic basis, since restoration of blood volume in depleted patients is a cardinal principle of surgery. A patient with a marked anemia or an ineffective circulating blood volume is one who has no reserve in the event of further severe bleeding. The work of Lyons and Mayerson [8] demonstrated the importance of the correction of anemia and diminished blood volume in order to avoid anoxia and its attendant damage to vital structures, retarded wound healing, and prolonged convalescence.

The proponents of the various views on the subject have repeatedly attempted to justify their opinions by an analysis of clinical material. In most instances, these analyses do not effectively indicate whether or not blood transfusions, in the presence of active bleeding, tend to prolong the bleeding, although the definite over-all impression is gained that blood transfusions are more beneficial than detrimental to a patient with an actively bleeding ulcer. Surprisingly little experimental work has been done on this problem. In fact, for many years the only experimental work directly relating to this question was that of Kordenat,[9] reported in 1930.

Kordenat's work consisted of experiments on only two animals. In each of two dogs, a sufficient amount of blood was withdrawn to result in mild hypotension. A small branch of the femoral artery was then severed and allowed to bleed until a clot formed. The previously withdrawn blood was then returned intravenously, restoring the arterial pressure to normal, and the pressure was further raised to hypertensive levels by the administration of epinephrine. In neither animal was there any recurrence of the bleeding. In the report of these experiments there was no mention made of the length of time the severed vessel bled or of the speed of administration of blood and saline. There were no apparent controls, and two experiments would seem to be insufficient basis for any conclusions. Consequently, the series of experiments reported herein was undertaken by us in an attempt to confirm and augment the work of Kordenat and thus to provide a more satisfactory experimental justification for the replacement of blood volume in clinical patients with active bleeding.

While the present work was in progress, Sachs and co-workers [10] reported experimental observations made for the same purpose. The methods used by this group were different in that one of the jejunal arteries and veins was severed in each animal, and, in some animals, clots were artificially formed by the application

7. Bowers, R. F., and Russett, N. E.: Bleeding Peptic Ulcer: Favorable Results by Conservative Treatment, Ann. Surg. **132**:690-701, 1950.

8. Lyons, C., and Mayerson, H. S.: The Surgical Significance of Hemoglobin Deficiency in Protein Depletion, J. A. M. A. **135**:9-10, 1947.

9. Kordenat, R. A.: The Relation of Blood Transfusion to the Disturbance of Blood Clot Formation, Mil. Surgeon **66**:206-213, 1930.

10. Sachs, A.; Wilhelmj, C. M.; Struck, H. C.; Waldmann, E. B., and McGuire, T. F.: Massive Gastro-Intestinal Hemorrhage: Experimental Observations, Gastroenterology **19**:113-117, 1951.

of trichloroacetic acid. Transfusion was not given until the clot had formed in each animal and, of six animals with natural clot formation, recurrent hemorrhage occurred in only one.

METHODS

Healthy mongrel dogs varying in size from 5 to 24 kg. were employed. Each animal was anesthetized with veterinary pentobarbital (nembutal®). A cannula connected to a mercury manometer was inserted in the exposed common carotid artery and continuous blood pressure tracings recorded on a smoked drum. A cannula was inserted in the left femoral vein for the administration of blood and fluids. The left deep femoral artery was widely exposed for the withdrawal of blood, and the blood withdrawn was collected in a bottle which received 10 cc. of 5% sodium citrate for every 90 cc. of blood. A very small length (average 2 mm.) of the right superficial femoral artery was exposed, great care being taken in the latter procedure to avoid extensive dissection around the vessel, which might result in excessive vascular spasm. In each experiment this vessel was severed transversely with a sharp knife, clamping or ligating the distal end and allowing the proximal end to bleed freely. Although blood was periodically removed from around the site of the bleeding by sponging, the vessel itself was not again touched, and no efforts were made to dislodge any clots forming around the mouth of the vessel. In two animals (Group I) the blood flowing from this vessel was collected and citrated and later reinfused after the bleeding had stopped. In these animals this blood loss was sufficient to cause a marked drop in arterial pressure, but in later experiments the blood flow from the superficial femoral artery alone was insufficient to cause significant hypotension, and it was necessary to withdraw blood from the profunda femoral artery. In 13 animals (Group II) the left profunda and right superficial femoral arteries were severed simultaneously, and, after the animal showed evidence of moderate shock, the profunda was clamped; in each case the blood transfusion was begun five minutes after bleeding from the superficial femoral vessel had ceased. In 13 animals (Group III) blood was withdrawn from the left profunda artery until moderate shock ensued; after this vessel was clamped and the blood pressure had stabilized, the superficial femoral artery was severed, and, at the same time, the reinfusion of previously withdrawn blood was started. In 18 of the animals in these three groups, saline was administered rapidly after completion of the blood transfusion. At the conclusion of each experiment, in most cases the animal was killed, and autopsy was performed. A few animals were used for other purposes. Another group of six animals (Group IV) served as controls; in this group only the superficial femoral artery was severed, and no blood or fluids were administered. The time necessary for bleeding to cease spontaneously was recorded in all experiments.

RESULTS

In these experiments it was found that there was a great variation in the amount of blood loss (expressed in percentage of blood volume, calculated according to the method of Ivy[11]) necessary to produce a significant degree of hypotension. The smallest relative amount lost was 21.7%, resulting in a fall in arterial pressure of 50 mm. Hg, and the largest was 46.6%, resulting in a fall of 80 mm. Hg. The blood pressure level after production of shock varied between 30 and 96 mm. Hg, as compared with an initial level between 80 and 180 mm. Hg. The average fall in pressure with blood loss was 75 mm. Hg, the average percentage of blood volume lost being 31.8%. Except in three animals (No. 4, 5, and 7), the blood pressure rose to levels approaching the initial blood pressure when the blood transfusion was completed (Table). Excluding these three animals, the blood pressure readings after trans-

11. Ivy, A. C.; Greengard, H.; Stein, I. F.; Grodins, F. S., and Dutton, D. S.: The Effect of Various Blood Substitutes in Resuscitation After an Otherwise Fatal Hemorrhage, Surg., Gynec. & Obst. **76**:85-90, 1943.

fusion in the other 25 dogs averaged 10 mm. Hg lower than the initial blood pressure level. Not all of the lost blood volume was restored, since the blood lost from the severed vessel was not collected in most cases.

The blood transfusions were given at variable rates, the slowest rate being 8 cc. a minute, and the most rapid being 57.1 cc. a minute. The latter transfusion resulted in death from apparent cardiac failure at the completion of the transfusion; at autopsy the heart was dilated, and moderate ascites and marked congestion of the liver were present. The average rate of blood administration for 28 animals was

Data From Groups I, II and III

Dog No.	Initial Blood Pressure (Systolic)	% of Blood Volume Lost	Systolic Blood Pressure After Withdrawal of Blood	Systolic Blood Pressure at Completion of Transfusion	Time of Bleeding from Severed Vessel, Min.
Group I					
1	120	28.8	60	120	30
2	160	32.3	50	100	12
Group II					
3	120	37.6	90	110	13
4	120	25.4	70	80*	12
5	130	23.7	40	50†	11
6	140	27.4	50	120	4
7	140	22.4	50	90*	15
8	130	29.9	40	110	10
9	120	35.1	60	100	8
10	120	34.6	50	100	2
11	160	28.1	50	100	15
12	120	31.9	30	110	7
13	130	41.5	50	120	5
14	100	32.9	40	100	6
15	110	39.2	50	100	3
Group III					
16	120	37.7	90	120	3
17	120	23.6	60	120	3
18	180	31.7	80	160	5
19	140	38.4	70	120	4
20	130	37.9	60	130	4
21	150	46.6	70	150	5.5
22	120	34.4	60	120	7
23	160	32.8	70	160	5
24	110	21.7	60	110	3
25	160	28.1	60	140	3
26	180	24.5	70	180	4
27	130	28.7	60	120	4
28	140	34.2	55	150	4

* Blood pressure dropped with homologous transfusion.
† Blood pressure never rose with transfusion; ? irreversible shock.

22.2 cc. a minute. When transfusions were given fairly slowly, there was a slow uniform rise in arterial pressure, but when the rate was rapid, there was a marked increase in pulse pressure, and if the transfusion was not slowed, there was a later tendency for the blood pressure to fall. This sequence of events was thought to be due to right heart failure.

In the animals in Groups I and II, the bleeding from the severed vessel ceased spontaneously in each case and did not recur during the autotransfusion. However, each of two of these animals (No. 4 and 7) was given 500 cc. of another dog's blood in addition, in an unsuccessful effort to create a hypertension; in each animal the

blood pressure fell when the homologous transfusion began. One of these animals (No. 4) became hyperpneic, the blood pressure fell, and bleeding from the severed vessel again took place; this was thought to represent an anaphylactic reaction to unmatched blood; autopsy revealed marked engorgement of the liver and moderate ascites. Young and co-workers [12] have pointed out the difficulties inherent in homologous transfusions in the dog.

In the Group-III animals, in which the autotransfusion was started at the same time that the superficial femoral vessel was severed, bleeding from the severed artery ceased spontaneously in each case and did not recur during the transfusion. A comparison of the length of time the vessels bled is extremely interesting. In Group II, this varied between 2 and 15 minutes, with an average of 8.5 minutes for the 13 animals; in this group, as in Group I, bleeding had ceased before transfusion was started. In Group III, in which blood was administered as soon as the vessel was severed, the time the bleeding persisted varied between 3 and 7 minutes, with an average of 4.2 minutes for the 13 animals. The average bleeding time for the control series (Group IV) of six animals was 4.0 minutes, with variations between 1.5 and 7 minutes.

After completion of the blood transfusions, large amounts (average 1,000 cc.) of isotonic sodium chloride solution were given at extremely rapid rates (average 110 cc. a minute) in 18 of the dogs in an effort to make these animals hypertensive. In only one animal (No. 1) was any significant degree of hypertension produced. However, in almost all these animals, variants of this picture developed, characterized by an initial elevation in pulse pressure followed by a drop in blood pressure, and, if the saline infusion persisted at the same rate, death ensued. This suggested heart failure, but at autopsy, although there was often moderate cardiac dilatation, the impressive findings were ascites, hepatic congestion, and the absence of pulmonary edema or pleural fluid. In one animal, the development of the hepatic engorgement was observed through a laparotomy incision. In two of these animals (No. 3 and 24) a recurrence of bleeding from the severed femoral vessel developed after rapid saline administration but without concurrent hypertension; in dog No. 24, this was a terminal event, but in dog No. 3, the bleeding stopped again five minutes later, and did not recur.

COMMENT

It is obvious that the conditions of these experiments are not analogous to the conditions associated with bleeding peptic ulcer, in which the digestive action of gastric juice, peristaltic and hunger contractions of the stomach, and the rigid fibrous tissue base of the ulcer all may play a part in prolonging hemorrhage. Nevertheless, these experiments seem to indicate that blood transfusions do not prolong bleeding from an open vessel. The comparisons of bleeding time further seem to indicate that citrated blood is of value in shortening the course of hemorrhage. While there was no significant difference between the bleeding times in the control series, and in Group III, in which transfusions were given concomitant with hemorrhage from the severed vessel, there was a comparative prolongation of bleeding times in Groups II, in which transfusion was not begun until after the bleeding had ceased. In this

12. Young, L. E.; Ervin, D. M., and Yuile, C. L.: Hemolytic Reactions Produced in Dogs by Transfusion of Incompatible Dog Blood and Plasma: Serologic and Hematologic Aspects, Blood **4**:1218-1231, 1949.

connection, the early work with sodium citrate, indicating that it causes paradoxical shortening of the coagulation time, when mixed with blood in vivo, should be recalled.[13] Of course, the use of large amounts of sodium citrate will result in a combination with calcium to such an extent that the clotting mechanism is completely disrupted.[14]

The superficial femoral artery was chosen because in all animals examined, this was comparable in size to the left gastric artery, which is the largest vessel that could be eroded by a bleeding ulcer. More commonly, such an ulcer erodes smaller branches.

The occurrence of liver congestion and ascites in the animals which received excessively rapid blood and saline infusions recalls the work of Kniseley and others,[15] indicating that there may be a sphincteric mechanism in the liver sinusoids, which, on contraction under certain conditions, produces splanchnic pooling. Whether or not a similar mechanism is present in the human is an open question. Certainly, this aspect requires further investigation.

SUMMARY

An experimental study is reported in which hypotension was produced by withdrawal of blood in a series of animals, and the effects of reinfusion of blood on bleeding from a severed artery were noted.

Under the conditions of these experiments there is no evidence that blood transfusion, however rapidly given, will cause a prolongation of bleeding from an open vessel, or that it will "blow out" a clot which is already formed in such a vessel.

13. Carter, W. S.: An Experimental Study of the Use of Sodium Citrate in the Transfusion of Blood by the Direct and Indirect Methods, South. M. J. **9**:427-439, 1916. Lewisohn, R.: A New and Greatly Simplified Method of Blood Transfusion, M. Rec. **87**:141-142, 1915. Neuhof, H., and Hirschfeld, S.: The Intramuscular Administration of Sodium Citrate: A New Method for the Control of Bleeding, Ann. Surg. **76**:1-8, 1922. Rosenthal, N., and Baehr, C.: Paradoxical Shortening of the Coagulation Time of the Blood After Intravenous Administration of Sodium Citrate, Arch. Int. Med. **33**:535-546, 1924.

14. Adams, W. E.; Thornton, T. F., Jr.; Allen, J. G., and Gonzalez, D. E.: The Danger and Prevention of Citrate Intoxication in Massive Transfusions of Whole Blood, Ann. Surg. **120**:656-669, 1944. Bruneau, J., and Graham, E. A.: A Caution Against Too Liberal Use of Citrated Blood Transfusions, Arch. Surg. **47**:319-325, 1943.

15. Kniseley, M.; Bloch, E., and Warner, L.: Selective Phagocytosis: I. Microscopic Observations Concerning the Regulation of the Blood Flow Through the Liver and Other Organs and the Mechanism and Rate of Phagocytic Removal of Particles from the Blood, The Royal Danish Scientific Association, Biological Writings, Vol. 4, No. 7, 1948. Thomas, W. D., and Essex, H. E.: Observations on the Hepatic Venous Circulation with Special Reference to the Sphincteric Mechanism, Am. J. Physiol. **158**:303-310, 1949.

TREATMENT OF NEUROGENIC URINARY AND FECAL INCONTINENCE IN CHILDREN

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ONE OF the most perplexing problems confronting the surgical staff of the Children's Hospital is the care of those youngsters who have congenital abnormalities of the lumbosacral portion of the spinal cord and consequent neuromuscular defects of the bladder and anal sphincters, which cause constant urinary and fecal soiling. While some of these children have normal, or near-normal, sensation and motor power of the legs, others have neuromuscular defects of marked degree in the lower extremities. Therefore the problem of urinary or fecal soiling of the perineum and thighs is doubly troublesome and disagreeable because the subject must wear leg braces, use crutches, or be handicapped in his locomotion and thereby unable to cleanse and care for himself properly. These children are wet, smelly, and uncomfortable; they rapidly become outcasts. Constantly soiled by their own excretions, they lead miserable lives, often are bedridden, and present such difficult and protracted nursing problems that home care is generally impossible; frequently, institutionalization must become their lot.

The present review summarizes our experiences in attempting to help 21 of these children, realizing that it would not be possible to restore any of them to normal yet feeling that it would be worth while to try to make their situations more tolerable.

CLINICAL DATA

All 21 children, ranging from 4½ to 10 years of age, had congenital defects of the lumbosacral area (myelomeningocele, sacral malformation, myelodysplasia, sacral agenesis, etc.) with obvious bony deformities of the lumbosacral spine, sacrum, or coccyx by roentgen examination and with a wide variety of neurological defects in the lower part of the trunk, the perineum, or the legs. Sixteen previously had had some form of neurosurgical operation for treatment of a meningocele or myelomeningocele, while two had had removal of lipomata from a deformed cauda equina. Seven of the children had had one or more orthopedic operation for improving the usefulness of the legs by tendon transplantation, tendon lengthening, stabilization of a foot, or correction of a varus, valgus, or cavus deformity. Thirteen of the patients could walk reasonably well without braces or crutches; they had only

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slight neuromuscular deficiencies in the legs. Four required braces or crutches for ambulation. Two children had complete flaccid paralysis of the legs. Two patients had no weakness of the legs. Two children had moderate hydrocephalus, but the process had been completely arrested. All the subjects had severe incontinence of urine or feces, or both. Although we have cared for other children with less severe degrees of incontinence, there were included in the present series only those whose situation was serious enough to demand the radical surgical procedures which are described.

Only 2 of these 21 youngsters were mentally retarded; the remainder were intelligent but were denied the right to attend school because of the strong urinary or fecal odor which constantly attended them in spite of the fact that they would be wearing several diapers, covered by rubber pants. Being constantly bathed in clothes which were wet with urine or with urine and feces, the skin of the genitalia, perineum, and thighs became extremely irritated in spite of the meticulous care which might be given by the mother. In several of the children, deep perineal, vulval, or scrotal ulcers developed, which became secondarily infected and showed little tendency to heal.

One child had a fairly normal anal tone; in all other patients it was obviously deficient. The anus was generally lax or patulous. Fecal soiling of the perineum, buttocks, and thighs was present in all cases. Not infrequently there was fecal impaction of the rectum and descending colon, with diarrheal fluid escaping around such masses.

A few of the children had dilated bladders, but they were completely insensitive to the overdistention and the overflow dribbling which existed; obviously, there was a neuromuscular imbalance with a greatly increased tone of the bladder sphincters. In all other patients there was urinary incontinence because of a weak or paralyzed bladder outlet. The urethras (of the females) were large, relaxed, and patulous; slight pressure in the suprapubic area would usually produce a gush of urine from the urethra. In a few instances the bladder was rather contracted and had completely lost its function as a reservoir. Though in some cases the urine was clear, generally there were varying degrees of urinary infection. By roentgenologic examination, hydronephrosis and pyelonephritis were common.

TREATMENT EMPLOYED

The multiplicity of operative procedures described in the literature for correction of neurogenic bladder incontinence suggests that no one of them has been completely satisfactory. Mertz and Smith [1] and Chute [2] favored exploration of the spinal cord and reported successful results following relief of traction or pressure from the cord structures. Although favorable results are obtained in an occasional case, the successes following this procedure are few. Ingraham reported on one patient from this hospital who had temporary relief, but later the original bladder dysfunction returned. Two patients in the present series obtained no benefit from removal of cauda equinal lipomas.

1. Mertz, H. O., and Smith, L. A.: Posterior Spinal Fusion Defects and Nerve Dysfunction of the Urinary Tract, J. Urol. **24**:41, 1930.

2. Chute, A. L.: The Relation Between Spina Bifida Occulta and Certain Cases of Retention, J. Urol. **5**:317, 1921.

Thompson and Jacobson [3] have observed good results following transurethral resection in children who are known to have a rim of hypertrophied tissue at the vesical orifice. Obviously, this form of therapy would be applicable only for the minority whose bladder dysfunction is caused by an overactive sphincter.

Numerous types of "artificial sphincters" have been fashioned from muscle or fascial slings; they have met with varying degrees of success but, on the whole, have not been too promising. Smith and Engel [4] employed the gracilis muscle, Goebell [5] used the pyramidalis muscle, and Ewert and Flint [6] turned down a strip of rectus muscle which was then passed around the urethra to aid in giving a sphincteric action. We have had little experience with such procedures; we doubt that they will have much permanent value.

TABLE 1.—*Ureteral Transplantation and Establishment of Wet Colostomy* *

Patient	Sex	Date of Operation	Procedure	Follow-Up
I. G.	F	1936	Plastic to rectum for incontinence; no relief	Died 1945; intestinal obstruction from adhesions
		1936	Fascial sling to anus; no relief	
		1937	Sigmoidostomy	
		1940	Ureters transplanted into the sigmoid giving a wet colostomy (Fig. 1*A*)	
C. O.	F	1940	Attempt to snug up bladder outlet; ineffective	After 1941, odor offensive for several years; now wears disposable bag; odor is no problem; well adjusted and happy; no pyelitis; October, 1951, had baby without difficulty
		1941	Transection of sigmoid, establishment of wet colostomy (Fig. 1*A*)	
D. H.	M	1941	Transection of sigmoid, establishment of wet colostomy (Fig. 1*A*)	1951, odor has always been considerable problem; no pain or pyelitis; some leakage from bag during night; considerable irritation of skin; sophomore in high school; seems to resent his deformity
J. M.	M	1942	Transection of sigmoid, establishment of wet colostomy (Fig. 1*A*)	Odor severe at first, much less troublesome later; 1951, wears rubber colostomy bag; skin clean; no pain; good adjustment; occasional bleeding from orifice; 1952, slight hydronephrosis; stone removed from left lower calyx

* Procedure used in treatment of urinary and fecal incontinence.

In some instances it is possible to plicate the bladder outlet to a degree sufficient to improve the control of urinary flow. Although we have had many disappointments with this, it has been successful in several cases (not included in the present series) in which the incontinence had been mild.

For four of our patients (Table 1) the urine was diverted into the colon (which ended as a colostomy) giving a wet colostomy, while in nine others (Table 2) the urine was run into an artificial bladder which had been constructed from a segment of the sigmoid, one end of which was brought out as a stoma on the anterior

3. Thompson, G., and Jacobson, C., Jr.: Neurogenic Vesical Dysfunction Due to Spina Bifida and Myelodysplasia, Am. J. Surg. **61**:224, 1943.

4. Smith, C. K., and Engel, L. P.: Neurogenic Vesical Dysfunction in Children, J. Urol. **28**:675, 1932.

5. Goebell, R.: Zur operativen Beseitigung der angeborenen Incontinentia vesicae, Ztschr. gynäk. Urol. **2**:187, 1910.

6. Ewert, E. E., and Flint, L. D.: Rectus Muscle Sling for Neurogenic Incontinence, Surgery **27**:688, 1950.

abdominal wall. These various rearrangements of the urinary and colonic tracts are indicated in Figure 1. It is not necessary to give here the case histories, the details of the individual operations, or the minutiae of problems of postoperative care; this mass of particulars would probably be confusing. It is more informative to sum-

TABLE 2.—*Establishment of Sigmoid Bladder,* Establishment of Colostomy†*

Patient	Sex	Date of Operation	Procedure	Follow-Up
M. L. S.	F	1941	Transection of sigmoid, establishment of wet colostomy (Fig. 1*A*)	1946, mucosal incrustations removed from wet colostomy; 1952, getting along rather well; wears 2 bags on the 2 orifices; occasional urinary leakage or odor from the urinary bag; no stones; no infection
		1947	Sigmoid bladder constructed; colostomy at a second orifice (Fig. 1*B*)	
M. F. P.	F	1942	Transection of sigmoid, establishment of wet colostomy (Fig. 1*A*)	1946, blood, diarrhea and severe anemia; 1951, stones removed from the sigmoid bladder; 1952, resides in a state hospital-school; good mental adjustment to her situation; occasional bleeding from the sigmoid bladder, odor not offensive
		1947	Sigmoid bladder constructed; colostomy at a second orifice (Fig. 1*B*)	
M. R.	F	1943	Loop colostomy, with ureters transplanted into distal, isolated, sigmoid segment (Fig. 1*C*)	Occasional bleeding from colostomy, only slight odor; died 1946, ? cause
J. H.	M	1943	Loop colostomy, with ureters transplanted into distal, isolated, sigmoid segment (Fig. 1*C*)	Addison's disease developed, ? cause, is on continued treatment for this; at first odor severe, but later less marked; 1952, wearing single rubber bag over the two openings, has slight leakage at night; no infection; getting along fairly well
J. E.	F	1943	Loop colostomy, with ureters transplanted into distal, isolated sigmoid segment (Fig. 1*C*)	1950, bilateral hydronephrosis, poor function of right kidney; 1951, colostomy situation is handled fairly well; mental retardation
B. H.	M	1944	Loop colostomy, with ureters transplanted into distal, isolated sigmoid segment (Fig. 1*C*)	Wears one bag over both openings; odor at first a problem, no longer so; 1951, good adjustment; goes to school; has chronic urinary infection, requiring chemotherapy; occasional bleeding from sigmoid bladder
J. R.	F	1944	Loop colostomy, with ureters transplanted into distal, isolated, sigmoid segment (Fig. 1*C*)	1945, stone removed from sigmoid bladder 1952, very well adjusted; uses disposable colostomy bags; well pleased; no odor, pain, or infection; occasional bleeding from mucosa
W. O.	M	1944	Loop colostomy, with ureters transplanted into distal, isolated sigmoid segment (Fig. 1*C*)	1952, resides in state hospital-school; occasional abdominal pain; has hydronephrosis on right, bag emptied every 4 hr.; most of the urine removed by catheter inserted into the sigmoid bladder every 4 hr.; good adjustment in school, mixes well; has stones in the sigmoid pouch
		1945	Closure of mesenteric defect following herniation of small intestine	
		1950	Closure of perforation of sigmoid bladder	
		1951	Closure of perforation of sigmoid bladder	
A. N.	F	1947	Sigmoid bladder constructed; continuity of colon maintained (Fig. 1*D*)	1951, general status excellent; very well adjusted; catheter fits snugly into sigmoid orifice; catheter opened every 3 hr. for release of urine

* For urinary incontinence.
† For fecal incontinence, in all cases except one.

marize the various experiences, pointing out what seemed to be helpful and what was undesirable in the different operative procedures.

The rearrangement depicted in Figure 1*A* is that which was tried for four patients with both urinary and fecal incontinence. The lower sigmoid was divided and its distal end closed; the proximal end of the sigmoid was brought out as a

permanent colostomy, and the ureters were transplanted into the upper sigmoid. This gave a "wet colostomy" through which both urine and feces were simultaneously discharged. With this rearrangement, by diverting all urine and fecal material from the perineal region so that these areas could be kept clean, dry, and sanitary, the patient was invariably and promptly improved. All previously existing cutaneous inflammations and ulcerations of genitalia, perineum, or thighs healed very promptly. For such relief the patients and their families were always very grateful. However,

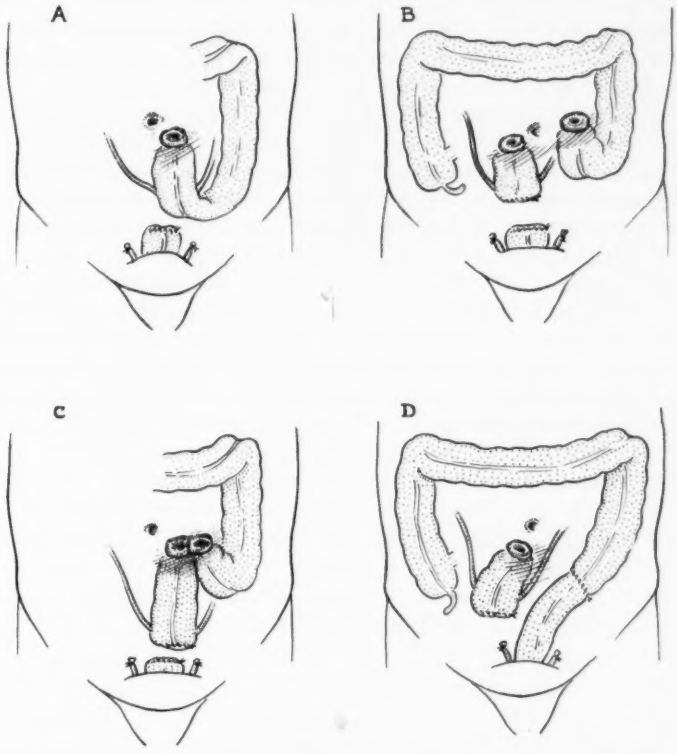

Fig. 1.—Methods employed for control of incontinence for patients listed in Tables 1 and 2. Methods *A*, *B*, and *C* were for therapy in cases in which there was both urinary and fecal incontinence. *D* was for a patient who had only urinary incontinence. *A*, division of lower sigmoid, with closure of its distal end. Ureters transplanted into proximal segment. Proximal end of the sigmoid brought out of anterior abdominal wall as a "wet colostomy." *B*, division of lower sigmoid, with closure of its distal end. Lower end of descending colon brought out as terminal colostomy. Ureters transplanted into sigmoid, which is used as a "sigmoid bladder." *C*, same general arrangement as *B*, but the two colostomy openings are placed close together on the abdominal wall so that they could be fitted into a single colostomy bag. *D*, ureters transplanted to sigmoid, which is used as an isolated "sigmoid bladder." Continuity of the sigmoid reestablished.

the establishment of a wet colostomy brought problems of its own. The intermixture of urine and feces was generally difficult to handle, there being a constant discharge of this material from the colostomy stoma, producing a persistent mess, particularly

previously when only a bag of rubber was available for the collection of such discharges. The rubber bags constantly had a disagreeable odor in spite of repeated washings. More recently, appliances have become available that utilize inexpensive disposable plastic bags which can be discarded when filled. With these disposable sacs, the odor problem has been almost completely eliminated. Our oldest patient with a wet colostomy is now 20 years of age. This young woman went through an uneventful pregnancy and delivery of a baby in 1951. She now works as a clerk in a department store. She is quite a happy and well-adjusted person. She uses the replaceable plastic colostomy bags; they cause little expense or inconvenience. This case illustrates what may be accomplished when the surgeon provides the patient with some sort of arrangement which can be taken care of fairly easily and when the patient is one who has a cheerful and realistic attitude toward her deformity.

Before the time that plastic colostomy bags were available, we had great tribulation from some of the wet colostomies because urea-splitting organisms produced from the urine a constant liberation of ammonia, which with its disagreeable odor was impossible or difficult to mask. Because of this factor, it seemed desirable in two patients to keep the bacteria out of the urine by separating the urinary and fecal streams (Fig. 1*B*), in spite of the fact that this would give two orifices on the abdominal wall. The lower sigmoid was divided and its distal end turned in. The sigmoid itself was used for the construction of a pouch to receive urine. The lower part of the descending colon was brought out as an end colostomy. In both patients in whom this arrangement was tried there was immediate relief from the soiling of perineum, buttocks, and thighs, for which the patients were most grateful. Although the odor problems were diminished or abolished, this arrangement was a little disturbing because there were two stomas on the abdominal wall to care for. In spite of such drawbacks, this general arrangement (when used in the early 1940's) appeared to be a distinct advance over the establishment of a wet colostomy. For one of these patients, the sigmoid bladder was cared for by the placement of a collecting bag over the presenting orifice. In the other, the orifice could be made snug enough so that it acted as an obstructive mechanism. However, the orifice was still large enough to allow the insertion of a catheter every few hours to withdraw the urine that had collected in the pouch. Observing that the latter means was much more satisfactory and agreeable to the patient, we had hoped to produce such a similar narrow orifice in all subjects who had sigmoid bladders but found it impossible to accomplish this with any regularity.

The arrangement shown in Figure 1*C* was used in six cases for treatment of patients who had both urinary and fecal incontinence. The lower sigmoid was divided and the distal end closed. The upper sigmoid was brought out as a loop colostomy (subsequently converted into two separate orifices), using the major portion of the sigmoid for an artificial bladder, into which the ureters were transplanted. This general arrangement was used in the hope that one colostomy bag could be employed to cover the two orifices, which were fairly close together, and still retain the advantage of keeping the urea-splitting organisms out of the urine (before the urine is discharged into the bag), thus minimizing the ammonia odor. This plan appeared to be somewhat better than that shown in Figure 1*A*, but we now feel that it really has little or no advantage over the wet colostomy.

Figure 1*D* depicts the operative procedure used for one child who had total urinary incontinence and a fair anal tone, which however was insufficient to allow transplantation of the ureters to the sigmoid and discharge of all urinary and fecal material by rectum. A segment of sigmoid was removed from the colonic circuit so that it could be employed as a sigmoid bladder after implanting the ureters into it; the continuity of the sigmoid was reestablished. The patient has gotten along very well during the five years that the sigmoid bladder has been used. There is a snug orifice so that a catheter can be passed into it each three or four hours by the child and the urine withdrawn. Between times there is no leakage of fluid from the opening. The whole picture has been extremely pleasing. However, we doubt if this arrangement is really much more satisfactory than that which could have been attained more simply by using the urinary bladder as a receptacle, as described in the following paragraph (wherein the urethra is closed off and a permanent cystostomy is established).

The use of a sigmoid bladder (such as depicted in Fig. 1*B*, *C*, and *D*) brought certain risks and complications: 1. While the segment of sigmoid was usually a redundant capacious receptacle and would receive much urine before discharging it to the exterior, in at least one instance there was constantly a marked spasm of this sigmoid pouch, which was extremely difficult to treat. There would be paroxysms of severe abdominal pain, and urine would shoot out under great pressure. It was impossible to control these attacks in spite of local instillation of anesthetics or soothing solutions or the administration of antispasmodics. 2. Many of the sigmoid bladders frequently collected calcarious deposits, some of which would be free within the lumina, while others were in the form of encrustations adherent to the mucosal lining, the removal of which was sometimes very traumatizing to the bowel wall. 3. In many of the sigmoid bladders there was ulceration and bleeding, which at times was of severe degree. 4. The greatest hazard occurred in one boy who on two different occasions perforated the sac, requiring emergency surgical closure thereof; the escape of urine into the general abdominal cavity produced peritonitis, intestinal obstruction, and a near fatality each time.

Having struggled through the trials of building sigmoid bladders and the tribulations of caring for these children thereafter, our experience now convinces us that the sigmoid bladder has certain advantages and also very real risks. A decade ago it appeared to be distinctly better than anything which was available at the time for the treatment of the child who had uncontrollable urinary incontinence. We now feel that such surgical reconstruction should no longer be used. This change in policy has been brought about by the current availability of such appliances as a Rutzen bag or modifications thereof, which can be cemented to the abdominal wall over a bowel stoma, and to which can be attached disposable plastic sacs. If properly fitted and used, such an apparatus can keep the patient clean and odorless. With this newer adjunct, we now feel that if urinary and fecal incontinence are so severe that it is necessary to divert both streams away from the perineum, it is simplest to establish a wet colostomy (Fig. 1*A*) because this can be managed by the patient in a reasonably satisfactory way.

For all eight patients listed in Table 3 there was severe urinary incontinence which required surgical relief, but it was felt that the fecal soilage could be handled, in spite of anal laxity, by properly cleansing the colon, giving a constipating diet,

and then washing out the bowel once daily with a cleansing enema. In this way it has been possible in these eight children to take care of the fecal excretions with fair satisfaction. This more recent experience in 1950, 1951, and 1952 makes us feel that probably some of the earlier patients, listed in Tables 1 and 2, might possibly have been treated without diverting their fecal streams out through a colostomy. We are inclined to believe that in the future it will rarely be necessary to establish a colostomy for the treatment of fecal incontinence because the more conservative measures seem to be adequate in providing the cleanliness which is desired.

TABLE 3.—*Division of Urethra and Establishment of Permanent Cystostomy* *

Patient	Sex	Date of Operation	Procedure	Follow-Up
R. L.	M	1946	Cystostomy; suprapubic closure of bladder outlet; leakage recurred	1950, because of greatly contracted bladder and difficulties in keeping catheter clean, bilateral ureterostomies done (elsewhere); kidney condition greatly improved thereafter
		1946	Perineal closure of urethra; leakage recurred	
		1946	Perineal excision of segment of urethra	
N. C.	F	1949	Cystostomy; perineal division of urethra; leakage recurred	1951, wears thigh rubber bag; some urinary odor; stones removed from bladder; patient well adjusted; mother pleased
		1949	Perineal division of urethra; leakage recurred	
		1949	Suprapubic division of urethra	
S. F.	F	1950	Cystostomy; suprapubic division of urethra	1951, is in state hospital-school; releases catheter every hour during day; on constant bladder drainage at night; no psychological problems
C. A.	F	1950	Cystostomy; suprapubic division of urethra without anesthesia	Mentally retarded; 1951, wears rubber thigh bag; no infection, pain, or stones; perineum dry; mother pleased
C. C.	F	1950	Cystostomy; suprapubic division of urethra; leakage recurred	1952, mild urinary infection; controlled fairly well with Gantrisin; wears rubber thigh bag; perineum dry; pleased with results
		1951	Suprapubic division of urethra	
C. D.	F	1950	Cystostomy; suprapubic division of urethra	1951, does not wear bag; releases catheter every 2-3 hours; no pain; infection, or stones; perineum dry; mother pleased
M. C.	F	1950	Cystostomy; suprapubic division of urethra; leakage recurred	1952, does not wear bag; releases catheter every 2-3 hours; perineum dry; mother pleased
		1950	Suprapubic division of urethra	
M. M.	F	1950	Cystostomy; suprapubic division of urethra	1952, wears rubber thigh bag in day; when infection or plugging of catheter occurs, uses Ruppel irrigator at night; perineum dry; pleased with results

* Procedure used in treatment of urinary incontinence.

In all the subjects listed in Table 3, the severe urinary incontinence was treated by surgical closure of the urethra and by establishment of a permanent suprapubic cystostomy (Fig. 2). In this way the bladder itself could be used as a urinary reservoir, or at least it could act as a channel through which urine was diverted outward into some kind of an external appliance. The child's genitalia, perineum, and thighs could be kept dry at all times. Every one of these children has been markedly improved because the perineum, vulva, thighs, and buttocks can be kept dry and clean; much has thereby been gained in their rehabilitation.

There have been difficulties in dividing the urethra in a manner which would not be followed by reestablishment of the channel. As indicated in Table 3, for four patients it was necessary to perform this step two or even three times before permanent closure of the bladder outlet was attained. It thus becomes obvious that interruption of a urethra is not a minor procedure which is to be taken lightly. We have now learned that it is always inadvisable to attempt division of the urethra in a female by a perineal approach, since it is almost impossible to get sufficient exposure to do it with facility. In all females the division should be done by a suprapubic route, completely dividing the urethra just beyond the bladder and then turning the bladder outlet inward with a row of interrupted silk stitches. These are then reinforced by an additional row of interrupted silk stitches, which turn the bladder farther inward. Only in this way can secure closure be assured. When the small mushroom catheter is placed in the bladder, we have attempted to put this in a very high position so that it might be kept away from the trigone and thereby reduce irritation.

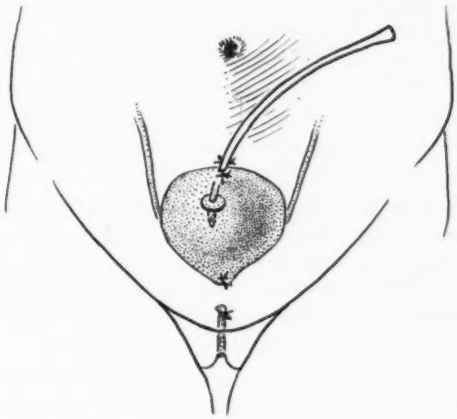

Fig. 2.—Method employed for control of urinary incontinence for those patients listed in Table 3. Posterior urethra is completely divided and closed off. Permanent cystostomy has been established.

Usually, the bladder catheter should be changed about once a month. Any existing or recurring urinary infections should be appropriately treated by chemotherapeutic agents. From time to time, if there is any important cystitis, a Ruppel irrigator can be connected with the catheter during the night so that the bladder can be lavaged and cleansed.

The permanent cystostomy can be handled in one of two ways. In most instances, the suprapubic catheter has been connected to a rubber bag, which is attached to the thigh so the child could be ambulatory. In other patients the urinary bladder has had a good capacity and no thigh bag has been used, the catheter merely being unclamped every few hours for release of urine. When there is extensive kidney damage, incompetence of the ureterovesical valves, or a bladder of a rather small capacity, it is best to leave the suprapubic catheter open at all times and connected with a rubber receptacle so that the urinary tract may be given the best possible

chance for function and for repair of damages which have been sustained previously. Whenever the kidneys are in a reasonably good condition, when there are competent ureterovesical valves, and when the bladder has a fair capacity, it is permissible and more aesthetic to avoid the use of a rubber urinary bag and to merely open the bladder catheter at appropriate intervals for the release of urine.

All these patients or their families have expressed gratitude for what has been accomplished; the child is dry at all times, and the rubber apparatus is not troublesome or distasteful to manage. Two of the children are ardent swimmers; they merely clamp off the short catheter and tuck it under the bathing trunks when they take to the water. Needless to say, such transformation from a miserable child into one who can thus enjoy life is a worth-while surgical attainment!

RECOMMENDATIONS

It is realized fully that these surgical attempts never end with entire satisfaction to the patient or to the surgeon, but they seem to be about the best that can be offered to these malodorous and unhappy children. Summing up our various experiences of the past, it would be our policy at present to treat patients with urinary and fecal incontinence (from lumbosacral neurological disturbances) according to the following general principles and with the following procedures.

1. It should be made quite certain that everything possible has been gained by any neurosurgical attack which might be used against a lumbosacral meningocele, spinal abnormality, or spinal cord tumor.

2. For those children who have only a mild urinary incontinence and who are beyond 3 or 4 years of age, attempts should be made to strengthen the bladder sphincter by active exercises in which the urinary stream is started and stopped, started and stopped, so that the child can be made conscious of this shut-off mechanism and can frequently exercise it consciously. Whenever there is severe laxity of the bladder outlet, such exercises are useless.

3. Whenever there is an "overflow" bladder, from excessive tone of the bladder sphincter, prolonged drainage (by cystostomy or by inlying urethral catheter) permits the bladder to shrink, to gain an increased tone, and to more effectively empty itself after such drainage is stopped. In some cases an attempt should be made to resect a portion of the bladder neck, hoping thereby to relieve partially the spasm of the bladder sphincters and permit the detrusors to empty the bladder more efficiently. Bladder-neck resections carry a variable outlook, which should be made known to the family beforehand. Some are rather successful in giving satisfactory bladder function; others make the situation worse by producing constant dribbling (which might require further radical operative therapy at a subsequent time).

4. For the patient who has considerable laxity of the anal or bladder outlets (or both) there should be no radical surgical steps for local repairs or for diversion of urinary and fecal streams until the child is at least 3 or 4 years of age. In a few instances, when there seems to be almost hopeless soiling in the first few years of life, some neuromuscular control does appear subsequently so that the situation is ameliorated to a considerable degree. Hence, every chance for spontaneous improvement should be given before any destructive or mutilating surgery is performed. If no important gain is evident by the time the child is 5 or 6 years of age, there is almost no chance of having it appear later.

5. Apparently, it will seldom be necessary to treat anal incontinence by establishment of a colostomy. The bowel usually is sluggish and has a reduced tendency to spontaneous evacuation. A child who has a lax anal sphincter and severe soiling can generally be carried along reasonably well (beyond 4 or 5 years of age) by the use of a constipating diet and by a daily cleansing enema. If the colon is allowed to accumulate large and inspissated fecal masses, there is passage of fluid material around this which gives constant soiling. On the other hand, if the bowel is kept free of such accumulations by proper cleansing, the colon usually moves only once a day (at the time of giving the enema), and there is little or no soiling between times. Certainly a long and concerted effort should be made at such conservative management before resorting to a colostomy. It is now our belief that a colostomy can be avoided in the vast majority of cases.

6. For a child who has great laxity of the bladder outlet and constant dribbling, it is generally desirable to attempt a plication of the bladder sphincters, using a retropubic approach and reefing in the dilated structure by grasping muscular tissues at the sides and pulling them forward and in front of the bladder outlet to reduce the size of its lumen. While most of these plications have been ineffectual in accomplishing very much, in a few patients urinary control has been established in this way. Certainly, it should be tried in all cases in which there is mild laxity of the bladder outlet before attempting destructive surgery, such as permanent drainage of the bladder, diversion of urine into a sigmoid bladder, or establishment of skin ureterostomies.

7. In those cases in which it is fully evident that urinary incontinence is irreversible, the child should be provided with some means to divert the urine so that the perineum and thighs can be kept dry. It is almost always impossible to transplant ureters into the sigmoid so that urine and fecal material can be discharged through the anus; the anus usually is too lax to give any satisfactory control over semifluid material. If both urinary and fecal streams have to be diverted away from the perineum, this can be done by establishment of a wet colostomy, which discharges both fecal and urinary materials (Fig. 1*A*). The intermixed fluid and feces can be collected in a colostomy bag which has been cemented to the abdominal wall and which has disposable plastic sacs.

8. It is generally unnecessary and, indeed, undesirable to construct a sigmoid bladder (Fig. 1*B*, *C*, or *D*). When urine has to be diverted from the perineum, generally this can be accomplished by severance of the urethra, closure of the bladder outlet, and establishment of a permanent suprapubic cystostomy (Fig. 2). When such tube drainage of the bladder has been established, the catheter can be kept clamped (but released every three or four hours) if there is competence of the ureterovesical valves and if there are fairly good kidneys. Conversely, the tube should be left open at all times and connected to a rubber bag on the thigh whenever there is incompetence of the ureterovesical valves or marked damage of the kidneys.

9. Whatever method of therapy is outlined and given for these subjects, the patients must remain indefinitely under the care of a physician or of a clinic that can guide them, alter the regimen, or care for those contingencies which almost certainly will arise from time to time.

SUMMARY

Attention is focused on the problem of children who, because of lumbosacral neural defects, have anal and bladder incontinence and severe soiling. These youngsters are constantly messy, malodorous, and uncomfortable. Before proceeding with the measures herein advocated, one must be convinced one is dealing with permanent and incurable incontinence. It is never possible to make these children normal, but much can be accomplished by various methods which will make them dry, less odorous, and much happier. The methods of therapy which have been employed for 21 patients are summarized, and the methods which are currently recommended are outlined.

STRANGULATED DIAPHRAGMATIC HERNIA

Report of Four Cases

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WHILE the frequency of strangulation in diaphragmatic hernias is not great, the complication is a fatal one demanding early surgical therapy. All physicians should be aware of this condition and consider it a possibility in any patient with lower thoracic or upper abdominal pain, the etiologic basis of which has not been clearly established.

I wish to present my experience with four cases and in outline form summarize a group of cases [1] collected from the literature since the report of Carter and

1. (*a*) Barrie, J., and Foreman, H. M.: Strangulated Traumatic Diaphragmatic Hernia, Lancet **2**:12, 1948. (*b*) Bastien, P.: Strangulated Diaphragmatic Hernia, Lille chir. **5**:258, 1950. (*c*) Codet, and Enel: Strangulation Revealing a Diaphragmatic Hernia in an 8 Year Old Child, Mém. Acad. chir. **77**:42, 1951. (*d*) Cooke, C. M., and Corner, B.: Recurring Left Diaphragmatic Hernia with Intestinal Obstruction by Adhesions, Proc. Roy. Soc. Med. **42**:914, 1949. (*e*) Candolin, Y.: On Diaphragmatic Hernia, Acta chir. scandinav. **95**:61, 1947. (*f*) Coulter, E. B.: Traumatic Hernia with Strangulation of Stomach, Northwest Med. **49**:267, 1950. (*g*) Diddle, A. W., and Tidrick, R. T.: Diaphragmatic Hernia Associated with Pregnancy, Am. J. Obst. & Gynec. **41**:317, 1941. (*h*) Dugan, D. J., and Samson, P.: Strangulation of the Stomach and Traumatic Diaphragmatic Hernia, J. Thoracic Surg. **17**:771, 1948. (*i*) Fishbach, H. R.: A Fenestra of the Diaphragm, Arch. Path. **6**:867, 1928. (*j*) Grumillier, H.: Strangulated Diaphragmatic Hernia, Mém. Acad. chir. **76**:567, 1950. (*k*) Hamilton, J. E., and Phillips, T. W.: Traumatic Hernia of the Diaphragm with Strangulation and Gangrene of the Stomach: Report of 2 Cases, Am. J. Surg. **78**:686, 1949. (*l*) Hughes, F.; Kay, E. B.; Meade, R. H., Jr.; Hudson, T. R., and Johnson, J.: Traumatic Diaphragmatic Hernia, J. Thoracic Surg. **17**:99, 1948. (*m*) Ismail, M. A.: A Case of Diaphragmatic Hernia with Strangulation, J. Egyptian M. A. **16**:674, 1933. (*n*) Lam, C. R.: Treatment of Traumatic Hernia of the Diaphragm, Arch. Surg. **60**:421, 1950. (*o*) Li, Y., and Li, C. Y.: Strangulated Diaphragmatic Hernia: Case Report with Necropsy, Chinese M. J. (Chengtu Ed.) **1**:77, 1943. (*p*) Lloyd, E. O., and Roberts, D.: Congenital Defect of Left Diaphragm with Volvulus of Stomach and Transposition of Viscera, Brit. M. J. **2**:485, 1947. (*q*) Moore, H. D.: Some Unusual but Instructive Surgical Emergencies, Brit. M. J. **2**:756, 1950. (*r*) Orr, I. M.: Acute Diaphragmatic Hernia Associated with Intestinal Obstruction, Brit. J. Surg. **34**:96, 1946. (*s*) Redon, H.: Traumatic Diaphragmatic Hernia with Immediate Strangulation, Mém. Acad. chir. **75**:588, 1949. (*t*) Shields, R. P.: Case of Strangulated Diaphragmatic Hernia, Brit. M. J. **2**:495, 1947. (*u*) Thompson, J. W., and LeBlanc, L. J.: Congenital Diaphragmatic Hernia: Visceral Strangulation Complicating Delivery, Am. J. Surg. **67**:123, 1945. (*v*) van Eeden, J., and Deneys, J. B.: A Case of Diaphragmatic Hernia with Obstruction, South African M. J. **20**:303, 1946. (*w*) Weeder, S. D.: Torsion and Volvulus of the Stomach with Diaphragmatic Hernia, Ann. Surg. **102**:382, 1935. (*x*) Wolfson, S. A., and Goldman, A.: Strangulating Diaphragmatic Hernia of the Liver: Report of Case with Surgical Care, Surgery **24**:846, 1948. (*y*) Yenen, E.: Case of Diaphragmatic Hernia Complicating Pregnancy, Türk tib cem. mec. **12**:236, 1946.

Giuseffi [2] in 1948. These authors presented in detail the clinical symptomatology and the physical and x-ray findings in strangulated diaphragmatic hernia, and these findings will be omitted from this presentation.

REPORT OF CASES

CASE 1 (Mrs. L. B., Seaside Hospital).—This case has been previously reported in detail.[3] The patient was a 32-year-old white woman. On Feb. 25, 1949, seven hours after a normal delivery, she began complaining of intermittent cramping pain in the left upper abdomen and in the posterior portion of the chest.

After physical examination and x-ray studies were completed, a diagnosis of diaphragmatic hernia with probable strangulation was made. Seven hours after onset of symptoms the patient was taken to surgery. The abdomen was explored through a left upper rectus incision. Only the descending colon and spleen were found in the peritoneal cavity, the remainder of the gastrointestinal tract being in the left pleural cavity, with the diaphragmatic defect in the posterolateral portion (pleuroperitoneal hiatus). The gastric wall was edematous and hemorrhagic, as was also the greater omentum. After reduction of the herniated organs, the margins of the diaphragm were freshened and approximated with interrupted sutures of No. 20 cotton. The abdomen was closed in a routine manner.

The patient had a normal convalescence and was discharged on the ninth postoperative day. On Dec. 18, 1950, Dr. Sterling Pillsbury delivered the patient of a normal infant by Caesarean section.

Comment.—Thompson and LeBlanc, in 1945, reported the first successful repair of a strangulated diaphragmatic hernia in the immediate postpartum period. Six fatalities due to strangulated diaphragmatic hernia complicating pregnancy are recorded in the literature. It is interesting to note that at least one patient with a known diaphragmatic hernia delivered three times without ill effect and, finally, in the fourth pregnancy, strangulation developed and she died.

CASE 2 (Mrs. V. C., Seaside Hospital).—A 72-year-old white woman entered the hospital at 5:20 a. m., March 22, 1949. Several years previously the patient had received several fractured ribs on both sides in an automobile accident. Her health had been fairly good until one week prior to admission when she began having dizzy spells. On the afternoon of March 21, the patient had a sudden severe pain in the epigastrium, with radiation to the right side of the chest and shoulder, and she fainted. She was seen by a physician at 4 a. m. and sent to the hospital. On admission she was dyspneic and complained of severe upper abdominal pain. Temperature was 98.4 F. and pulse rate 100, and she appeared acutely ill. About 9 a. m. she went into shock. She was placed in an oxygen tent and given plasma. X-rays of the abdomen and chest taken shortly after admission were read about 9 a. m., and diaphragmatic hernia was suspected (Fig. 1). By 11 a. m. the patient had sufficiently recovered from shock to permit further x-ray examination (Fig. 2). This examination confirmed the diagnosis of right diaphragmatic hernia with intestinal obstruction. The white blood cell count was 19,750, with 91% polymorphonuclear leucocytes and 118% hemoglobin. The electrocardiogram was read as showing evidence of possible old coronary infarction.

The patient was taken to surgery at 2:45 p. m., and with use of intratracheal anesthesia, the abdomen was opened through a right rectus incision. The hernia could be palpated behind the right lobe of the liver. The incision was carried across the right eighth interspace and the pleural cavity entered. A large quantity of dark bloody fluid and a loop of mahogany-colored ileum were present in the right pleural cavity. The diaphragmatic defect was enlarged and the ileum returned to the peritoneal cavity. With the liver displaced caudally, the diaphragm was repaired with interrupted sutures of No. 20 cotton. A catheter was introduced through the ninth interspace and the chest closed. Approximately 5 ft. (152 cm.) of gangrenous ileum

2. Carter, B. N., and Giuseffi, J.: Strangulated Diaphragmatic Hernia, Ann. Surg. **128**:210, 1948.

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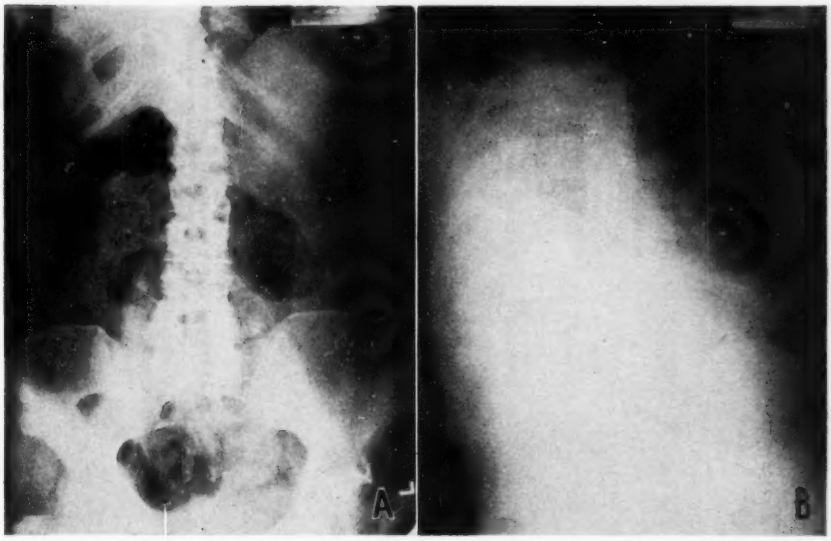

Fig. 1 (Case 2).—*A*, scout roentgenogram of abdomen. There are several loops of gas-filled bowel extending up along right lateral chest wall, presumably between lateral margin of liver and chest wall. There is some gaseous distention of intestinal tract, which suggests possibility of mechanical intestinal obstruction. *B*, roentgenogram of chest. There is diffuse haziness of right chest, which is suggestive of two gas-filled loops of intestine in lower portion of right chest.

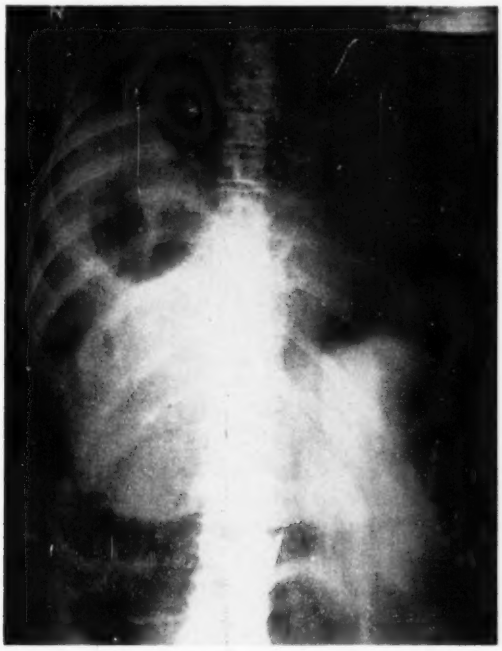

Fig. 2 (Case 2).—Roentgenogram of chest and abdomen. There is dense homogenous opacity of lower portion of right lung field. There is crescent-shaped shadow of air density in lower portion of right lung field. Heart, trachea, and mediastinal structures are shifted toward left. Distended loops of intestine are seen in abdomen.

TABLE 1.—*Summary of Cases of Strangulated Diaphragmatic Hernia Since Reports of Carter and Guiseffi*

Year	Author	Age, Yr.	Sex	Type	Organs	Side	Operation	Result	Autopsy	Incision	Comment
1928*	Fishbach [11]	26	F	Congenital	Colon, stomach, spleen, pancreas	Left	No	Died	Yes	..	18 days post partum
1933*	Ismail [1m]	48	M	?	Colon, omentum	Left	Yes	Recovery	....	?	Diagnosis acute intestinal obstruction, omentum congested
1935*	Weeder [1w]	65	M	?	Small intestine, omentum, stomach	?	No	Died	Yes	..	Diagnosis perforated ulcer, stomach hemorrhagic
1941*	Diddle and Tidrick [1g]	23	F	?	Stomach, small intestine, colon	Left	No	Died	Yes	..	Died in labor, stomach strangulated with perforation, third pregnancy
1942*	Li and Li [1o]	23	M	Traumatic	Stomach, colon, and spleen	Left	No	Died	Yes	..	Died 16 hours after admission
1945	Thompson and LeBlanc [1u]	31	F	Congenital	Stomach, intestine and pancreas	Left	Yes	Recovery	....	Abdominal	Pancreas showed fat necrosis
1946	Orr [1r]	19	F	Congenital	Stomach, transverse colon	Left	Yes	Recovery	....	Thoracic	Hernia recurred, several operations
1946	Yenen [1y]	17	F	Congenital	Stomach, small intestine	Left	No	Died	Yes	..	Small intestine showed areas of infaretion, fat necrosis
1946	vanEeden and Deneys [1v]	40	F	Congenital	Stomach	Left	Yes	Recovery	....	Abdominal	Acute symptoms 24 hr.; volvulus of intra-abdominal portion with strangulation of stomach
1947	Shields [1t]	61	M	?	Small and large intestine	Left	No	Died	Yes	..	Autopsy, 9½ ft. small bowel and 14 in. colon strangulated; hemothorax
1947	Lloyd and Roberts [1p]	6 mo.	M	Congenital	Stomach, small and large intestine, spleen	Left	No	Died	Yes	..	Volvulus of stomach
1947	Candolin [1e]	29	M	?	Splenic flexure	Left	Yes	Died	....	Abdominal	Colon wall gangrenous; colostomy; died 4th postoperative day
		23	F	Congenital	Stomach, small and large intestines, spleen	Left	Yes	Died	....	Abdominal	6 mo. pregnant, section done; volvulus of stomach with strangulation
1948	Barrie and Foreman [1a]	22	M	Traumatic (shrapnel)	Omentum, ⅓ small intestine, 45 cm. colon	Left	Yes	Died	Yes	Abdominal	Died on operating table; 45 cm. gangrenous colon
1948	Dugan and Samson [1h]	24	M	Traumatic (stab)	Stomach	Left	Yes	Recovery	....	Thoracic	Stomach blue black; onset two years after injury
		..	M	Traumatic (stab)	Stomach	Left	Yes	Recovery	....	Thoracic	⅓ of stomach in chest
1948	Hughes and co-workers [1i]	..	M	Traumatic	Colon	Left	Yes	Recovery	....	Thoraco-abdominal	12 hr. after jump from truck, gangrene of colon, double barrel colostomy

1948	Wolfson and Goldman [1x]	47	F	Congenital	Liver	Right	Yes	Recovery	....	Thoracic	Herniated liver was edematous; decreased in size after release
1949	Hamilton and Phillips [1k]	37	M	Traumatic (stab)	Stomach	Left	Yes	Recovery	....	Thoracic	Fundal portion of stomach gangrenous; resected, fistula
		38	M	Traumatic (auto)	Stomach	Left	Yes	Died	Yes	Thoracic	Portion of stomach gangrenous, resected second operation 10th day, pulmonary embolus
1949	Redon [1s]	50	M	Traumatic	Stomach	Left	Yes	Recovery	....	Thoracic	Volvulus of stomach containing 1 liter of hemorrhagic fluid
1949	Cooke and Corner [1d]	6 wk.	F	Congenital	Duodenum to sigmoid	Left	Yes	Recovery	....	Abdominal	3 in. of ileum strangulated; recurred age 4 yr. with obstruction
1950	Grumillier [1j]	55	M	Traumatic (stab wound)	Colon	Left	Yes	Recovery	....	Thoracic	12 in. of colon strangulated; acute intestinal obstruction 48 hr.
1950	Bastien [1b]	25	M	Traumatic (shrapnel)	Splenic flexure	Left	Yes	Recovery	....	1st, abdominal; 2d, combined	1st operation transverse colostomy; one month later hernia repaired
1950	Coulter [1f]	..	..	Traumatic (auto)	Stomach, small and large intestine	Left	Yes	Recovery	....	Thoracoabdominal	Organs bluish color; operation one month after accident
1950	Lam [1n]	62	F	Traumatic (auto)	Stomach, small and large intestine	Right	Yes	Recovery	....	Thoracic	18 in. small intestine strangulated
1950	Moore [1q]	16	M	Traumatic	Colon and omentum	Left	Yes	Recovery	....	Combined	Age 16 mo., thoracotomy for empyemia; symptoms 10 days
		36	F	Congenital	Stomach, splenic flexure, and spleen	Left	Yes	Died	Yes	Abdominal	Perforation at cardioesophageal juncture in hernial ring
1951	Codet [1c]	8	M	Traumatic	Transverse colon, omentum	Left	Yes	Recovery	....	Combined	Fall from a carriage 1 yr. previously
1952	Pearson	31	F	Congenital	Stomach, small and large intestine	Left	Yes	Recovery	....	Abdominal	Onset of symptoms 7 hr. after delivery
		72	F	Traumatic (auto)	Ileum	Right	Yes	Recovery	....	Thoracoabdominal	5 ft. of gangrenous ileum resected
		54	F	Parahiatal	Stomach	Left	Yes	Died	Yes	Thoracoabdominal	Entire stomach gangrenous; died 6th postoperative day
		89	F	Parahiatal	Stomach	Left	Yes	Recovery	....	Abdominal	Volvulus of stomach; acute symptoms 6 hr.

* Cases reported prior to 1945 but not recorded by Carter and Guise...

was resected and intestinal continuity restored by a side-to-side anastomosis. During the operation 500 cc. of whole blood and 500 cc. of 5% glucose in water were administered. During the first 24 hours after operation, 1,000 cc. of whole blood and 500 cc. of plasma were administered. She was in an oxygen tent for the first three days. She made a slow but steady recovery and was discharged on April 20, 1949. Figure 3 is a minature chest x-ray taken April 18. She has remained well and active since her discharge.

TABLE 2.—*Mortality in Seventy-Four Cases of Strangulated Diaphragmatic Hernia*

Years	No. of Cases	No. Operated	No. of Operative Deaths	Operative Mortality, %	No. Not Operated	Deaths	Nonoperative Mortality, %
1798-1805	11	0	..	....	11	11	100
1900-1919	7	7	5	71.4	..	..	..
1920-1929	10	7	3	42.8	3	3	100
1930-1939	6	4	1	25	2	2	100
1940-1949	29	23	6	26	6	6	100
1950-1952	11	11	2	18.1	..	..	...
Total.....	74	52	17	32.6	22	22	100

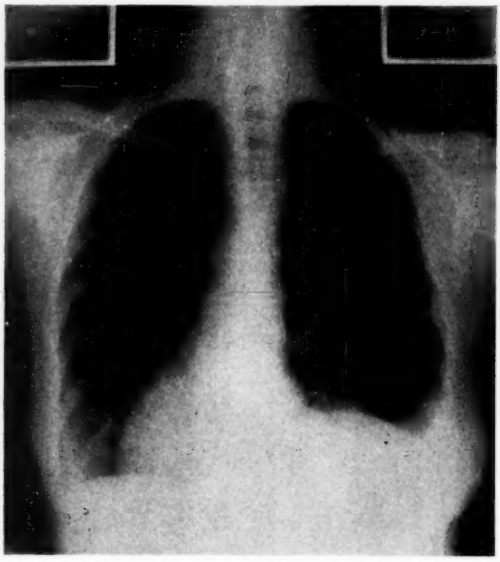

Fig. 3 (Case 2).—Miniature roentgenogram of chest, taken April 18, 1949.

Comment.—The above case is an example of traumatic hernia on the right side, resulting from an automobile accident several years previously. Right-sided traumatic diaphragmatic hernia is exceedingly rare. Lam reported a similar case. This case also illustrates how important it is to suspect strangulated diaphragmatic hernia in any patient with upper abdominal and chest pain for whom the diagnosis is not clear, and especially if there is a history of a previous injury to the chest or abdomen.

CASE 3 (Mrs. G. D., Seaside Hospital).—This patient was a 54-year-old white woman admitted to the hospital on April 7, 1949. Her chief complaints were nausea, vomiting, and diarrhea following the ingestion of sardines. Ten days before admission the patient had a similar but milder attack of abdominal distress. She gave a history of gall-bladder trouble for years. There was no previous surgery and no accidents. She had four children.

The present illness began one an one-half hours after the patient ate sardines for lunch on the day of hospital admission. She experienced extreme nausea and vomiting followed by mild prostration. The nurse at the plant where she worked gave her kaopectate® (a liquid preparation of kaolin and pectin), without relief. She was then given a hypodermic and sent to the hospital. On admission her temperature was 99 F., pulse rate 80, and respirations 20. Cremosuxidine® (a liquid preparation of suxidine, pectin, kaolin, and chocolate-mint flavor) and an enema were given, with some relief of symptoms. At 4:45 p. m., she was given meperidine (demerol®) hydrochloride for pain and had a small emesis. The nurse's notes at 10:00 p. m. stated, "Sleeping; no pain or nausea." At 4:00 a. m., on April 8, 1949, the patient was again given meperidine for pain in the stomach and back, and she again vomited. Examination notes at 8:00 a. m. recorded the following: shallow breathing, dyspneic, anxious, and strained look; lung fields clear to percussion and auscultation; abdomen tender in the epigastrium and in the right upper quadrant.

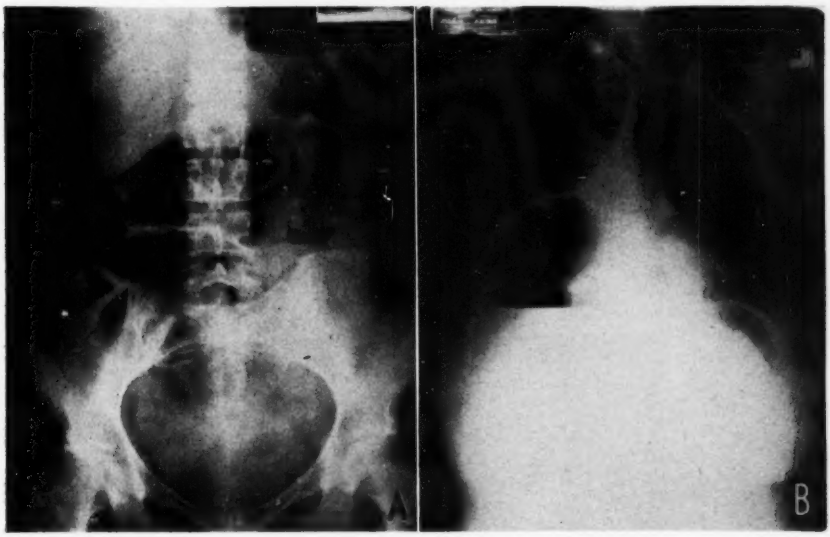

Fig. 4 (Case 3).—*A*, scout roentgenogram of abdomen. Considerable amount of gaseous distention is seen in colon, There is large collection of gas high up in abdomen. This may represent gas in stomach, but findings are not definite because entire gas shadow is not included in film. *B*, roentgenogram of chest. Large ovoid shadow of air density about 9 cm. in diameter is seen in lower half of right thorax. This air density has lower margin which is horizontal and apparently represents an air-fluid level. There is also an air bubble overlying left side of heart, with lower margin consistent with air-fluid level.

X-rays of the chest and abdomen were ordered (Fig. 4), also repeat blood count and electrocardiogram. The white blood cell count was 11,800, with 70% polymorphonuclear leucocytes, and the electrocardiogram was essentially normal.

When the above x-rays were read, the patient was taken to the x-ray department and additional x-ray studies made (Fig. 5). The nurse's notes at 10:30 a. m. stated, "patient still having pain in epigastrium; 11:00 a. m., vomiting."

The patient was seen in consultation at noon and surgery for strangulated diaphragmatic hernia advised. She did not appear acutely ill. The patient's blood was typed and cross matched, and she was given 1,000 cc. of 5% glucose solution.

With use of intratracheal anesthesia, surgery was started at 1:20 p. m. and completed at 5:00 p. m. A right upper rectus incision was first made. The stomach was not in the peritoneal cavity, and the hernia was felt in the region of the esophageal hiatus. It was impossible to reduce the stomach. The abdominal incision was then carried across the right eighth interspace, and, much to our surprise, the stomach was not in the right pleural cavity; however, a large

mass could be palpated in the mediastinum on the right side. The hernial ring was enlarged, and, with traction from below and pressure through the chest, the stomach was reduced. The entire stomach was in the mediastinum, with the exception of approximately 2 cm. of the pylorus. The entire gastric wall was black, and the cardia was exceedingly thin. It contained a large quantity of fluid and gas, which was removed by suction trochar. The left coronary ligament was incised and the left lobe of the liver retracted for adequate exposure. The hernia was repaired with interrupted sutures of No. 20 cotton. During this time the circulation of the stomach did not improve, and it was evident that an almost total gastrectomy would be necessary. The distal portion of the stomach was divided immediately proximal to the pyloric muscle, and the cardia was divided at its juncture with the esophagus. Because of the great stretching which had occurred, it was possible to accomplish an end-to-end anastomosis.

A stab wound was made in the right ninth interspace for catheter drainage. The right diaphragm was closed with interrupted cotton sutures. The intercostal incision was then closed with cotton sutures and the abdominal incision closed with through-and-through sutures of steel wire.

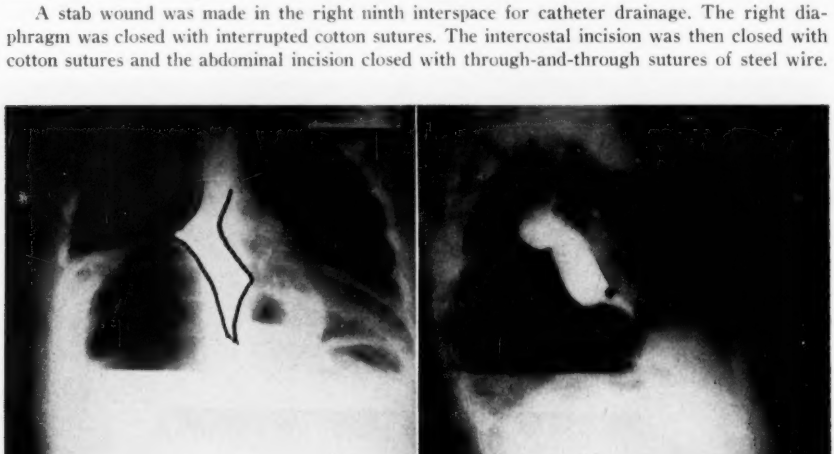

Fig. 5 (Case 3).—*A*, barium swallow. Flow of barium in esophagus was obstructed at level of seventh dorsal vertebra, and no barium entered stomach. (Photograph was retouched to outline barium in esophagus.) *B*, lateral view of chest after oral administration of iodopyracet (diodrast®). The more liquid solution is obstructed at same level as barium.

During the operation the patient received 2,000 cc. of whole blood and 1,500 cc. of plasma. Her blood pressure at the end of the operation was 90 systolic and 60 diastolic. Immediately upon return to her room she was placed in an oxygen tent. Despite intensive therapy the patient's systolic pressure remained below 100 for 48 hours, and the urinary output was depressed. By the third postoperative day the blood pressure was 130/90 and the renal function was improved. However, from the time of surgery the respirations were labored and gasping in character. Portable x-rays of the chest suggested pulmonary congestion. The patient died on April 14, the sixth postoperative day.

Microscopic Report of Resected Stomach.—The mucosa was necrotic, the nuclear structure was absent, and there were dark-brown pigmented deposits in the mucosa.

Autopsy Findings.—There was 500 cc. of serosanguineous fluid in the abdominal cavity. The peritoneal surfaces were glistening and smooth. The entire stomach had been resected and an end-to-end anastomosis made between the esophagus and duodenum. The anastomosis was intact. Over the surface of the pancreas small specks of yellow-fat necrosis were visible. In

the pleural cavity there was a fist-sized bulging of the mediastinal pleura on the right side, beginning at the esophageal hiatus, and a smaller bulge on the left side, the size of a small egg. Both sacs contained blood clots. The mediastinal pleurae were hemorrhagic. All lobes of the right lung were noncrepitant to subcrepitant throughout and purple-red on the cut section. The left lower lobe was subcrepitant and purple-gray on the cut section.

Comment.—It is remarkable that this patient could have such an extensive gangrene of the stomach with so few symptoms and findings. Hamilton and Phillips, in 1949, reported two cases of gangrene of the stomach due to strangulated diaphragmatic hernia. They collected four other such cases. We have not found any report of gangrene of the entire stomach caused by diaphragmatic hernia.

This case again emphasizes how important it is to consider strangulated diaphragmatic hernia in any patient with pain in the upper abdomen and lower chest

Fig. 6 (Case 4).—Roentgenogram of abdomen, posteroanterior view. Left diaphragm is not visualized.

when the diagnosis is not established, regardless of how vague and indefinite the symptoms may be.

Case 4 (Mrs. E. S., St. Mary's Hospital).—This 89-year-old woman was admitted to the hospital on March 20, 1952. At 3 p. m. on the day of admission she experienced sudden acute upper abdominal pain, with radiation under the sternum. The patient was seen in consultation at 6 p. m. The past history was difficult to obtain because of a speech impediment. She had been confined to a wheel chair for several years because of arthritis.

Examination showed an elderly obese woman propped up in bed and in obvious pain. There were tenderness and guarding in the epigastrium. Suggestive peristalsis was heard in the left axilla. The temperature was 98.6 F. orally; pulse rate, 90, and blood pressure, 105/60 (normal for the patient, 150/90). The white blood cell count was 14,400, with 85% polymorphonuclear leucocytes and 30 stab forms.

On examining x-rays of the abdomen (Fig. 6), the left diaphragm could not be identified, although the right diaphragm was visible. An x-ray of the chest (Fig. 7) was then taken, and

an abnormal air shadow with a fluid level was seen behind the cardiac shadow. The patient was then given a barium solution by mouth (Fig. 8), and this demonstrated the cardia and fundus above the diaphragm, with volvulus of the distal portion of the stomach.

The patient was taken to surgery at 9 p. m. and the abdomen entered through an upper midline incision. The serosa of the intra-abdominal portion of the stomach was injected. The proximal portion of the stomach had entered the mediastinum through a paraesophageal hernia 6 centimeters in diameter. This was reduced and the peritoneum excised from the hiatus. The crura were approximated snugly about the esophagus with interrupted sutures of No. 20 cotton. The abdominal wall was closed in a routine manner. The patient received 500 cc. of whole blood and 500 cc. of 5% glucose in water during the surgery.

The patient had a normal convalescence and was discharged from the hospital on the 10th postoperative day.

Fig. 7 (Case 4).—Roentgenogram of upright chest, posteroanterior view. Large air bubble with fluid level seen below cardiac shadow. Left diaphragm is not well visualized. Pneumograph was recorded in outline at bubble.

Comment.—The stomach is frequently involved in diaphragmatic hernia of both traumatic and nontraumatic types. Strangulation is almost always produced by the rotation of the stomach on its long axis. In spite of the patient's age and any associated condition, early surgery, rather than conservative management, was elected. It is our impression that the successful outcome resulted from the course of action.

SUMMARY

Four cases of strangulated diaphragmatic hernia are described. In one of these was the hernia traumatic in origin, although in a great majority of the recorded cases the hernia is of traumatic origin. In the traumatic case the hernia was on the right side, which is exceedingly rare. In one case the patient had gangrene of the entire stomach, necessitating total gastrectomy.

The importance of early diagnosis and surgical intervention has been emphasized.

Twenty-seven cases of strangulated diaphragmatic hernia have been collected from the literature since 1948, which, with my four cases, brings the total number of recorded cases to 74.

It is encouraging to note that the operative mortality is steadily improving.

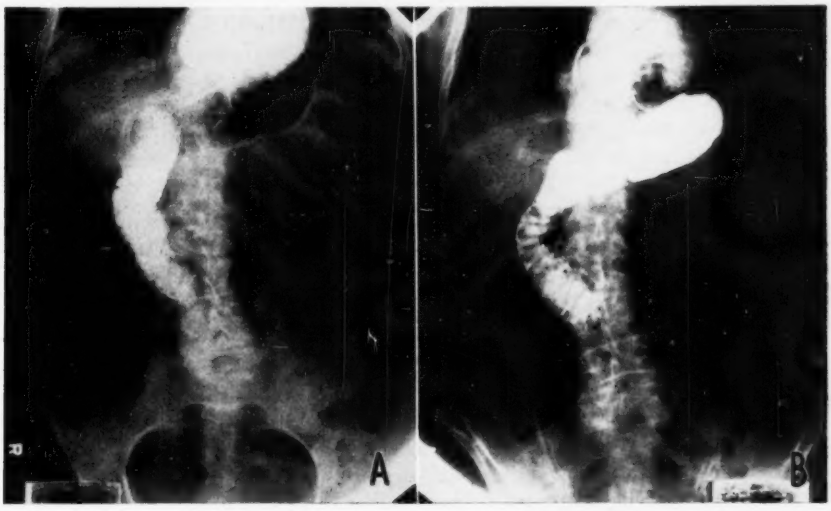

Fig. 8 (Case 4).—*A*, posteroanterior view of abdomen, with barium swallow. In this position barium solution would not pass from thoracic stomach into pars media (abdominal portion of stomach). Duodenal loop is widened because of cephalad displacement of proximal half of duodenum. *B*, posteroanterior view of abdomen, with barium swallow. In rotating patient onto her abdomen, barium passes from thoracic portion of stomach to abdominal portion. While patient was prone, barium solution could not be made to pass from pars media to thoracic portion of stomach, indicating complete volvulus.

ADDITIONAL REFERENCES

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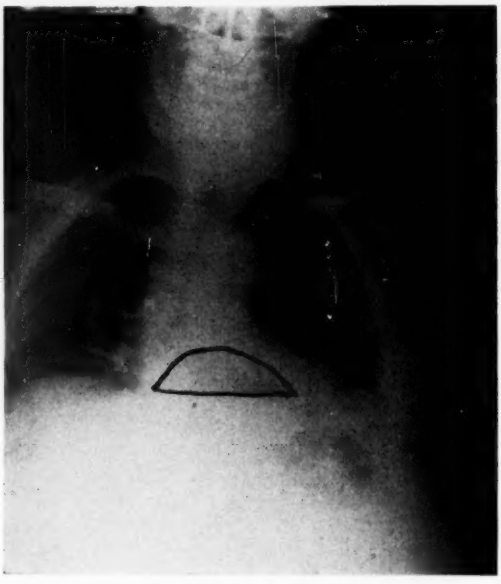

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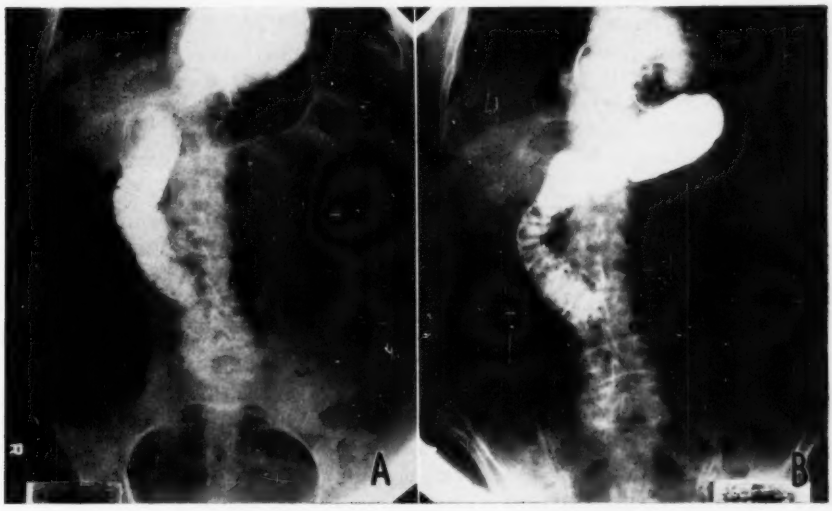

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ACUTE BOWEL OBSTRUCTION

Forty Years After Blunt Trauma

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THE LITERATURE contains numerous examples of blunt trauma to the abdomen which has resulted in injuries to all the viscera—not excluding even the gastric vessels [1]—but especially to the spleen, liver, kidney, bowel, and diaphragm. Little has been written, however, about delayed effects of the serious crushing injury upon which immediate operation has not been performed.

Spellberg and Ochsner [2] in seeking a relationship between nonpenetrating trauma to the small bowel and regional enteritis, traumatized the small bowel of dogs at laparotomy by crushing. Autopsy on survivors several months later revealed marked adhesion formation with large ropes of fibrous tissue and compression of the bowel.

The most extensive reference found on the remote sequelae to blunt injury to the bowel is in Küttner's book, "Die Spätschädigungen des Darmes nach stumpfer Bauchverletzung" [3] in which the literature is covered up to 1930. In 207 references to abdominal injury, only 21 cases of secondary stricture of the intestine are found, 2 of the duodenum and 19 of the ileum and jejunum.

Schloffer's [4] experiments indicate that strictures may result from fairly extensive trauma to the wall of the bowel or to the mesentery. If injury to the bowel predominates, then the ensuing stricture may be due to submucosal or subserosal hemorrhage, chyloma, or herniation of the mucosa into a split in the muscularis and/or serosa. If the injury occurs in the mesentery, a mesenteric hematoma may dissect into the wall of the bowel and cause fibrosis, or so injure the vessels that the intestine suffers from lack of circulation and fibrosis ensues.

Schloffer [4] cites cases in which complete obstruction occurred in three months to a few years following trauma. It is of interest that he states, "The true stricture of the intestines following blunt trauma to the abdomen occurs only in the small bowel, and has never been observed in the large."

From the Department of Surgery, St. Mark's Hospital.

1. Gambier, R.: Trauma chiuso dell'addome con rottura dell'arteria gastrica destra, Gior. veneto sc. med. **16**:325-327 (Aug.) 1942.

2. Spellberg, M. A., and Ochsner, A.: The Role of Trauma as a Possible Etiologic Factor in Regional Enteritis: Effect of Non-Penetrating Trauma on Small Intestine of Dogs, Am. J. M. Sc. **213**:579-584 (May) 1947.

3. Küttner, H.: Die Spätschädigungen des Darmes nach stumpfer Bauchverletzung, in Payr, E., and Küttner, H.: Ergebnisse der Chirurgie und Orthopädie, Berlin, Springer-Verlag, 1930.

4. Schloffer, H.: Über traumatische Darmverengerungen, Mitt. Grenzgeb. Med. u. Chir. **7**:1-137, 1900.

Fig. 1.—Preoperative roentgenogram of abdomen.

Fig. 2.—View at operation, showing distention of ascending colon, cecum, and terminal ilium. Note normal small and large bowel.

REPORT OF A CASE

R. J., a 56-year-old man, entered the hospital with acute onset of colicky pains in the right lower abdominal quadrant. They soon vanished, only to recur intermittently over the next two days. On the morning of the third day, signs of obstruction prompted the taking of the x-ray pictured in Fig. 1.

A laparotomy was performed through a lower right rectus incision, which revealed a large cecum 12 cm. in diameter, a normal appendix bound down in the lateral gutter with the thin congenital coverings of a Jackson's veil, and hard thick (3 to 5 mm.) bands of grey scar tissue coursing from the ascending and transverse mesocolon to the lateral and posterior abdominal wall (Fig. 2), compressing the upper ascending colon. These bands were rather avascular and easily freed from the bowel by sharp dissection, permitting the compressed colon to assume a more normal position.

Fig. 3.—Roentgenogram taken six weeks after operation shows bowel filled with barium enema.

No other pathological condition was found; hence the appendix was removed and the abdomen closed. Convalescence was uneventful.

Comment.—Inasmuch as no apparent etiologic agent could be found for the fibrous tissue at operation, we questioned the patient closely regarding abdominal injury. He could think of none until the third day postoperatively, when he suddenly recalled that when in his middle teens the rear wheel of a loaded manure wagon had gone over his abdomen, causing severe pain. He was kept in bed a week; then, from midspring until late fall, he walked doubled in half because of pain. He distinctly recalled watching ball games from the ground with his legs and back propped up on the other boys' clothing.

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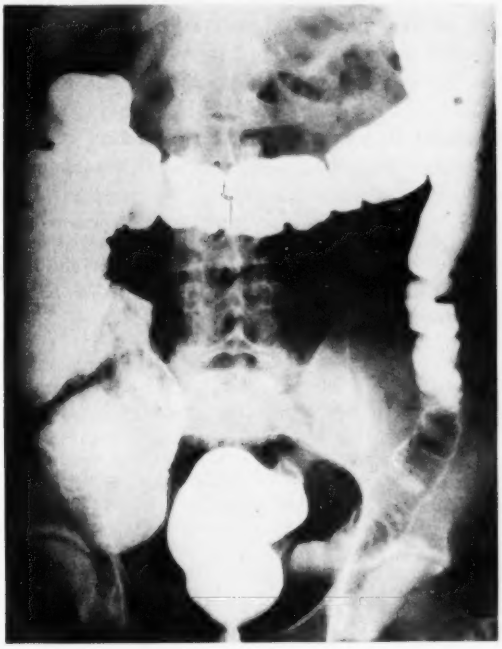

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A few weeks after the operation both the patient and his wife commented upon the fact of the extreme postoperative regularity of his bowels. In the light of this fact they concluded that the irregularity of the bowel, that they were now able to recall, must have been intermittent attacks of constipation. This observation concurs with that of Küttner,[3] when he suggested that etiology of stricture of the intestines after a blunt injury is "usually based on anamnesis." In the absence of obvious reasons for the scar tissue at surgery, the history of the wagon wheel may be assumed to be its origin.

An interesting phenomenon giving symptoms paralleling the above case is that of the congenital pericolic membrane.[5] These membranes have caused obstruction. They differ from the fibrous bands in the above case in that they resemble mesentery and are often well vascularized. They have definite lines of cleavage, however, and are easily removed, whereas the fibrous material in this patient had to be removed by sharp dissection.

SUMMARY

A case is presented in which complete obstruction of the ascending colon occurred as the probable sequela of blunt trauma to the abdomen sustained some 40 years previously.

5. Bigelow, W. A.: Study of Cause of Right-Sided Abdominal Pain in So-Called Chronic Appendicitis: Review of 1027 Cases, Canad. M. A. J. **23**:22-23 (July) 1930. Cashion, W. R.: Pericolic Membranes, Radiology **34**:66-68 (Jan.) 1940. Duffield, W. L.: Pericolic Membranes, Ann. Surg. **96**:98-101 (July) 1932.

ACUTE APPENDICEAL ABSCESS SIMULATING CECAL NEOPLASM

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AND
LAWRENCE ANDRESON, M.D.
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COEXISTENT cecal neoplasm with appendicular abscess is rather rare. In 1946 McLaughlin [1] in a review of the literature found only 11 such cases and added 1 of his own. In 1951 Hellsten and Ramström [2] of Sweden described four more cases. Thus we should be ever mindful of the fact that the differential diagnosis between an abscess in the right lower quadrant and cecal neoplasm should be made, if possible, in order to institute appropriate surgical therapy. In fact, the surgeon should be prepared to carry out ileocolic resection before laparotomy. In addition, when an appendiceal abscess is drained, one must be sure to reoperate at a later date in order to exclude any malignant growth.

REPORT OF A CASE

A 42-year-old man, a worker in a rubber factory, was admitted to the Somerville Hospital on Jan. 8, 1951, with a history of sudden constipation of two days' duration. At that time he took a tablespoonful of magnesium sulfate, with good results. However, two days later he again had a similar episode. This was rather unusual for him because he had had regular and well-formed bowel movements every morning as far as he could remember. This constipation was accompanied by lower abdominal colicky pain without nausea or vomiting. At the same time the upper abdomen became distended. Fairly recently he did remember having suffered occasional pyrosis. On one occasion he experienced some vague pain in the lower right quadrant. At no time did he have any regurgitation, vomiting, bloody or tarry stools, or any diarrhea. There was no loss of weight, no loss of strength, and no fatigue. In fact, he continued to work every day up until admission to the hospital.

Physical Examination.—The examination disclosed only a slightly distended abdomen with many tinkling metallic sounds in all quadrants.

X-Ray Studies.—These studies showed a constriction at the midascending colon; the probability of either cancer or an inflammatory lesion was considered (Figure).

Laboratory Examination.—Blood studies showed 5,110,000 red cells; 108% hemoglobin (Dare); 11,550 white cells, with 78% neutrophiles, 19% lymphocytes, 2% monocytes, and 1% eosinophiles. There was slight variation in the size of the red blood corpuscles. The urine examination was essentially negative. Nonprotein nitrogen was 30 mg. per 100 cc.; serum proteins 7.2 gm. per 100 cc.; blood chlorides 0.45 mg. per 100 cc., and acid phosphatase 1

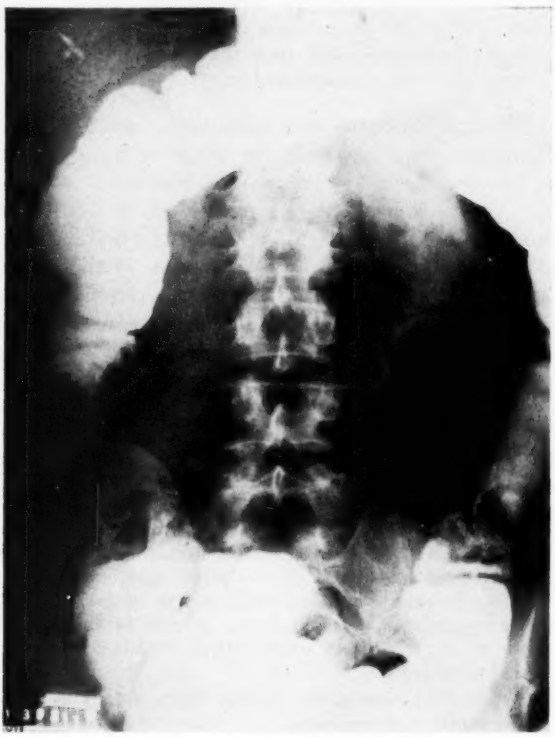
From the Somerville Hospital (Dr. Ciampa, Junior Surgeon; Dr. Miles, Head of the Department of Surgery, and Dr. Andreson, Head of the Department of Radiology).

1. McLaughlin, E. F.: Carcinoma of Cecum in Association with Acute Appendicitis, Am. J. Surg. **72**:585-593 (Oct.) 1946.

2. Hellsten, H., and Ramström, S.: Coexistent Cecal Cancer and Appendicular Abscess, A. M. A. Arch. Surg. **62**:112-117 (Jan.) 1951.

Bodansky unit. The serologic reaction for syphilis was negative. The stools were normal in character and consistency. There was no gross or occult blood.

Operation.—On Jan. 29, 1951, after the patient had been thoroughly prepared for a possible anastomosis, the abdomen was opened by a right paramedian rectus incision extending 3 in. (7.6 cm.) above and below the umbilicus. When the abdominal cavity was entered, a large mass of fairly thick fibrinous adhesions was found over the anterior surface of the midascending colon and part of the cecum. This mass was pulled toward the under surface of the liver, causing an angulation of the colon—the apparent cause of the mechanical obstruction. All adhesions were carefully dissected free, commencing at the hepatic flexure and continuing downward toward the cecum. When the cecum was exposed, the appendix was found to be enveloped and covered



Roentgenogram showing constriction at midascending portion of colon.

by a great many adhesions, some extending from the ileum to the cecum. The appendix was liberated and found to be arch-shaped, with one end, apparently its base, arising from the inner medial aspect of the cecum near the ileocecal junction and its distal end incorporated within the lowermost medial portion of the ascending colon. Apparently the appendix had ruptured with its tip into this lowermost portion of the colon. The appendix was totally removed, the base being left. As the tip was being freed, it became separated from the colon, thus leaving behind a gaping opening within the bowel wall. This opening was sutured in three layers, the last being reenforcing Lembert. Penicillin, 1,000,000 units, was sprayed into the cecal fossa, and the abdomen was sutured in layers. The patient made a good immediate postoperative recovery.

Pathologic Examination of the Appendix.—Gross Examination: The appendix was in two pieces and measured approximately 5 cm. in length and 1.3 cm. in diameter. The serosa was

reddened and showed some thin fibrous adhesions. The appendix had been incised, disclosing in the proximal portion a thick pale wall, a thick nodular yellowish mucosa, and a small lumen. What appeared to be the tip had been squeezed and on section showed approximately the same picture.

Microscopic Diagnosis.—The diagnosis was subacute and chronic appendicitis with chronic granulomatous nonspecific periappendicitis.

Postoperative Course.—The patient made an uneventful recovery and went home on the ninth postoperative day.

A barium enema repeated six months later disclosed a normal bowel.

SUMMARY

A case has been presented of an appendiceal abscess with resolution and rupture into the ascending colon. The similarity to cancer with obstruction is shown in the x-ray plate. Preparation had been made for a possible ileocolic resection and anastomosis prior to operation, a fact brought out by the possibility of coexistent cecal neoplasm.

COMPLETE HOMOLOGOUS HEART TRANSPLANTATION

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BRIAN A. COOKSON, M.B., Ch.B.(Edin.)
CHARLES P. BAILEY, M.D.
RUTH APPLER, R.N.
AND
FRANK RAJKOWSKI, B.S.
PHILADELPHIA

THERE have been previous experimental attempts to transplant hearts from one animal to another.[1] However, these transplants consisted of merely placing a donor heart in some portion of the recipient's vascular system, and at no time did the donor heart perform the function of maintaining complete circulation in the recipient animal.

We have been working with hypothermia as a method to allow a direct approach to intracardiac surgery, without the use of a complicated heart-lung apparatus.[2] By the use of hypothermia we have been able to completely stop all circulation for periods up to 30 minutes without subsequent morbidity or mortality. It occurred to us that such a period of time would be more than ample to perform a complete transplantation of the heart—removal of the recipient animal's heart and the substitution by a donor heart.

At present we have successfully performed complete transplantation of the heart in three dogs, with survival up to six hours postoperatively, during which time the circulation was sufficient to allow the return of normal reflexes, and electrocardiographic studies were apparently normal.

TECHNIQUE

Two rather small dogs of similar size were anesthetized with intravenous injections of thiopental (pentothal®) sodium and then placed in an ordinary beverage cooler for the production of hypothermia. Animal temperatures were lowered to 21 to 25 C. rectally. Respiration

This work was supported by U. S. P. H. Grant 394, and the Mary Bailey Foundation for Heart and Great Vessel Research.

From the Experimental Surgical Laboratory of the Division of Surgery, Department of Thoracic Surgery, Hahnemann Hospital and Hahnemann Medical College.

1. Mann, F. C.; Priestley, J. T.; Markowitz, J., and Yater, W. M.: Transplantation of the Intact Mammalian Heart, Arch. Surg. **26**:219, 1933. Marcus, E.; Wong, S., and Luisada, A. A.: Homologous Heart Grafts: Transplantation of the Heart in Dogs, in Forum on Fundamental Surgical Problems: Surgical Forum, 1951; Proceedings of the Forum Sessions, edited by O. H. Wangensteen, Philadelphia, W. B. Saunders Co., 1952.

2. Cookson, B.; Neptune, W. B., and Bailey, C. P.: Experimental Surgery Under Hypothermia, to be published.

was maintained by oxygen delivered through an endotracheal tube by means of a M. S. A. Pneophore respirator.[3]

After the body temperature was lowered sufficiently, the animals were removed from the cooler and prepared for surgery. A midline, sternum-splitting, thoracoabdominal incision was utilized for exposure. The azygos vein was ligated and transected near the superior vena cava. After this, the entire heart and both lungs were completely mobilized, care being taken to prepare sufficient lengths of superior and inferior vena cavae, the ascending aorta, and the trachea. After this was performed on both animals, the heart and lungs were removed from the donor animal, vascular clamps being used on all vessels. Then the recipient animal's heart and lungs were removed and the donor organs substituted.

The plan of substitution consisted of rapidly anastomosing the two ends of the ascending aorta by a continuous everting mattress suture of 5-0 nonabsorbable surgical (black silk) suture material. Then the ends of the superior vena cava were connected over a piece of polyethylene tubing, and partial circulation was resumed. An endotracheal tube was then placed in the trachea for respiration, and, finally, the inferior vena cava was connected over polyethylene tubing, at which time complete circulation was restored.

After the heart was in good condition, as evidenced by electrocardiographic studies, the tracheas were anastomosed end to end, and the cavae were individually clamped, the polyethylene tubes removed, and suture anastomosis performed.

After this, the diaphragm was repaired (during the mobilization of the heart and lungs, the phrenic nerves were preserved), and the chest was closed, using an intercostal catheter connected to a water seal drainage bottle.

After surgery, the electrocardiogram was visualized on the oscilloscope and periodic tracings were made. The animals were rewarmed to normal body temperature and observed for recovery, as noted by return of reflexes and respiration.

COMMENT

Using hypothermia of 21 to 24 C. rectally, we have an opportunity of stopping all circulation for about 15 minutes without any subsequent morbidity; this much time has been sufficient, once the heart and lungs are mobilized, to substitute the organs and connect the aorta and superior vena cava and resume respiration. This allows partial circulation for preservation of the central nervous system, and in an additional short period the inferior vena cava is connected to produce a complete circulation. We have had difficulty connecting the aorta over polyethylene tubing, since the aortic wall is rather friable, so that this anastomosis is made at once. By keeping the heart and lungs together, the problem of the pulmonary circulation is solved, and we know that homologous lung transplants will function satisfactorily for a rather long period of time.[4] In addition, by keeping the pulmonary circulation intact, the coronary circulation is maintained throughout the procedure. After the heart is in good condition, the remaining anastomoses of the trachea and cavae can be performed at leisure. We have not found it necessary to use heparin; in fact, under hypothermia there is a decreased coagulability of the blood, which returns to normal with elevation of body temperature.[2]

EXPERIMENTAL RESULTS

Experiment 1.—In this animal the cardiac action was not too satisfactory after transplantation. After surgery was completed, the cardiac action persisted for 30 minutes. The electrocardiogram revealed a high take-off of the S-T segment, and there were large inverted T waves in leads II and III (Fig. 1).

3. Manufactured by the Mine Safety Appliances Co., Pittsburgh 8.

4. Neptune, W. B.; Bailey, C. P., and Weller, R.: Experimental Lung Transplantation, to be published.

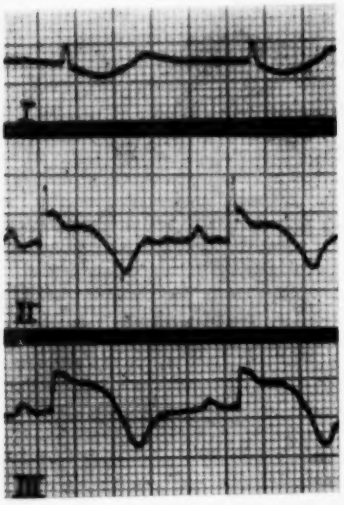

Fig. 1.—Electrocardiogram of dog which survived 30 minutes following transplantation of heart.

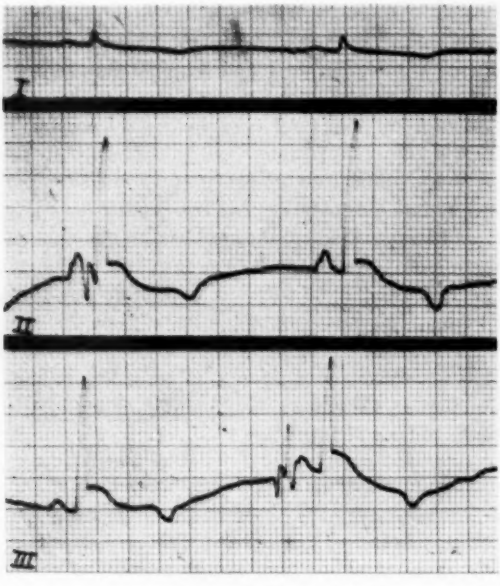

Fig. 2.—Electrocardiogram of dog which survived four hours following transplantation of heart.

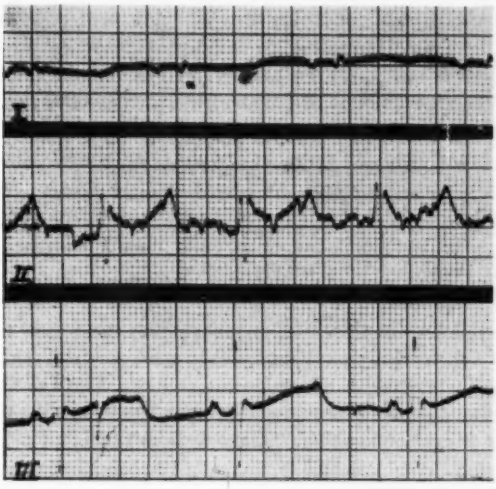

Fig. 3.—Electrocardiogram of dog which survived six hours following transplantation of heart.

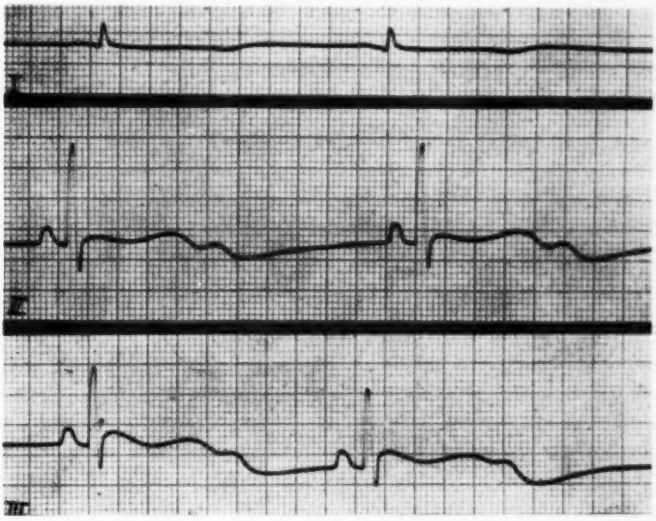

Fig. 4.—Essentially normal electrocardiogram of dog under hypothermia (22 C. rectally). There is normal sinus rhythm, with average rate of 30 beats a minute. QRS is 0.08 seconds, and there is a prominent S wave in lead II. Q-T interval is 1.2 seconds and T waves are upright but notched.

Experiment 2.—During the operative procedure, ventricular fibrillation developed in the animal and was successfully defibrillated. After transplantation the cardiac action appeared very good. There was a return of reflexes (pupillary and knee jerk) and the animal appeared to be improving when an agonal muscular spasm suddenly developed, and the animal died four hours following surgery. Autopsy revealed a large amount of blood in the pleural cavity, and the source of hemorrhage was found to be a small leak in the posterior suture line of the aorta. The electrocardiogram (Fig. 2) revealed a wide QRS complex in lead II and the amplitude of the QRS was increased in leads II and III. There was a high take-off of the S-T segment in lead II, and the T waves were inverted.

Experiment 3.—This animal had apparently normal cardiac action following transplantation, as evidenced by the electrocardiogram, and had return of reflexes and spontaneous respiration. Normal body temperature was restored, and the animal did very well for six hours following surgery, at which time it died. The cause of death was never fully explained, other than probable shock. The electrocardiogram (Fig. 3) revealed a normal sinus rhythm. The QRS complex was of normal duration and was of the prominent S type. There was a high take-off of the S-T segment, and a high monophasic T wave in lead II. The Q-T interval was 0.6 second.

SUMMARY AND CONCLUSIONS

We are presenting the first complete transplantation of the heart in dogs.

Three cases are presented in which the heart and lungs were successfully transplanted under hypothermia, with the donor heart maintaining all circulation and allowing return of reflexes, spontaneous respiration, restoration of normal body temperature, and survival up to six hours following surgery.

Although this is an experimental procedure, it demonstrates some of the potentialities of surgery performed under hypothermia. In addition, it is an ideal way of obtaining a completely denervated heart, as well as lungs, for physiologic study.

HOMOLOGOUS HEART GRAFTS

I. Technique of Interim Parabiotic Perfusion
II. Transplantation of the Heart in Dogs

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SAMUEL N. T. WONG, M.D.

AND

ALDO A. LUISADA, M.D.

With the Technical Assistance of W. C. Liu, M.D.

CHICAGO

THE TRANSFERRAL of tissue from one animal to another animal of the same species is a homologous transplantation, or homotransplantation. Transferral of tissue from one part of an animal to another part of the same animal is known as autotransplantation. Transplantation of tissue from an animal of one species to an animal of another species is heterologous transplantation. The problem of homologous transplantation of tissue is not one of laboratory research alone, for there are increasing demands for its solution and clinical application. A reasonable prolongation in time of survival of homotransplants would solve temporary problems of many types; permanent survival could be, in the words of Dempster and Lennox,[1] revolutionary.

The technique of transplantation of biologic material is many years old. A form of skin graft for cosmetic reasons was practiced in India in ancient times. In early modern times the practice of blood transfusion is an example of the transplantation of a tissue. Success has been attained with blood transplantation by detailed study of group specificities of this tissue. Tissue culture is another form of transplantation, since biologic material is grafted onto a foreign medium, albeit in vitro; this medium represents a new environment, designed to simulate that of the living animal's liquid menstruum, without the ability to defend itself antigenically.

Experimental transplantation of tissues is done in order to study the vital functions of the living cell, the more complex function of a tissue (a collection of cells with a similar purpose), or the function of an organ (a collection of tissues performing a specific body function). Previous research in the field of transplantation has produced several different types of grafts. With the exceptions of cartilage, blood vessels, cornea of the eye, and certain endocrines, all homologous transplants have been found to undergo complete disintegration at varying time intervals. Homologous grafting of endocrine glands is an example of the implanta-

Chicago Surgical Society 1952 Prize Paper, read before the Society, May 2, 1952.

From the Department of Surgery and the Laboratory of Cardiology, Chicago Medical School.

1. Dempster, W. J., and Lennox, B.: An Experimental Approach to the Homotransplant Problem in Plastic Surgery: The Use of Multiple Donors, Brit. J. Plast. Surg. **4**:81, 1951.

tion of a tissue, which is then left to the uncertainty of development of a blood supply from surrounding host tissues through the processes of granulation and organization. In 1909 Halsted [2] enunciated the principle that an endocrine transplant is more likely to be successfully transplanted when a deficiency of that gland exists in that host. Homologous skin grafts have been used as temporary grafts to cover open surfaces of seriously ill patients. Much of the basic and important experimental and clinical work on homologous skin grafts has been done by Medawar,[3] in England. The discussion of general principles involved in the attempted solution of problems arising in the course of this work leans heavily on his published works and great knowledge in the field. Other forms of grafts have served the purpose of a conduit only, examples being the grafts of artery and vein and of bone and cartilage. Grafts of blood vessels have been shown to undergo organization and fibrosis and ultimately replacement by tissues of the host. In the interim, they have served the purpose of a necessary conduit for the passage of blood. Bone grafts undergo osteoclastic activity and then form the nidus for osteoblastic activity by tissues of the host. For these clinically useful applications, banks of blood vessels and of bone are duly popular. The autologous grafting of less important nerves to bridge gaps in more important peripheral nerves is another example of the performance of the conduit function, since the transplanted nerve is useful only for the direction of the interrupted axones along the desired pathway.

Theories advanced to explain the disintegration of homologously transplanted tissues have been propounded by experimental surgeons and genetoimmunologists since the time of John Hunter. In our generation, Medawar [3] and Dempster,[4] of Great Britain, are preeminent in the field. Both these scholars favor the theory of an actively acquired immunity to explain destruction of the biologic foreign body. Homologous transplantation of tissues can be shown to be successful in the plant kingdom and in the lower strata of the phylogenetic scale, including invertebrates and the lower vertebrates, but becomes increasingly unsuccessful as one ascends the phylogenetic ladder. Ontogenetically, the embryo has little or no resistance to grafted foreign tissue. Whether this is due to inability to produce antibodies or to an inactive reticuloendothelial system is yet to be proved. Teleologically, the ability of a body to defend itself against an invading foreign tissue is a useful faculty. In humans, homologous transplants are satisfactory only in the uniovular (identical) twins.

Well known to workers in this field is the fact that the less highly specialized a tissue, the more is transplantation feasible, that is, the greater the "take." Conversely, the more specialized a tissue is, the more difficult is it of transplanta-

2. Halsted, W. S.: Auto- and Isotransplantation, in Dogs, of the Parathyroid Glandules, J. Exper. Med. **11**:175, 1909.

3. Medawar, P. B.: Immunity to Homologous Grafted Skin: Suppression of Cell Division in Grafts Transplanted to Immunized Animals, Brit. J. Exper. Path. **27**:9, 1946; Immunity to Homologous Grafted Skin: Relationship Between Antigens of Blood and Skin, ibid. **27**:15, 1946; Immunity to Homologous Grafted Skin: Fate of Skin Homografts Transplanted to Brain, to Subcutaneous Tissue, and to the Anterior Chamber of the Eye, ibid. **29**:58, 1948.

4. Dempster, W. J.: Problems Involved in the Homotransplantation of Tissues, with Particular Reference to Skin, Brit. J. Med. **2**: 1041, 1951; Observations on the Behaviour of the Transplanted Kidney in Dogs, Ann. Roy. Coll. Surgeons England **7**:275, 1950. Dempster, W. J.; Lennox, B., and Boag, J. W.: Prolongation of Survival of Skin Homotransplants in the Rabbit by Irradiation of the Host, Brit. J. Exper. Path. **31**:670, 1950.

tion, that is, the less likely is the "take." The problem which we attempt herewith to explore can then be stated as follows: Can a combination of highly specialized tissues, including (1) the syncytium of the myocardium, (2) the special conduction apparatus of the heart, including the Purkinje tissue, and (3) a complete system of blood vessels—all of these things constituting a highly specialized organ, the heart—be grafted in a mammalian animal? Can such a graft live in a homologous environment? Can such a graft actually function by receiving and delivering blood? Whether it might so function as to replace its counterpart in the host is a matter of speculation and investigation for the future. On the other hand, such a grafted heart might serve as a test object for physiologic and pharmacologic studies. The inherent automaticity of the heart only makes the possibility of study of such a test object more intriguing.

There is one report in the American literature on this problem. Mann, Priestley, Markowitz, and Yater [5] published a preliminary report in 1933 without detailed protocol or statistics and with no follow-up in the literature to date. They worked with a heart that was completely deprived of blood supply during the process of transplantation. In 1948 Sinitsyn [6] published an article in the Russian literature, suggesting a similar approach. The first results of our study were briefly presented in 1951 [7] and in 1952.[8]

EXPERIMENTAL PROCEDURE AND TECHNIQUE

The following principles of procedure were found to be most conducive to best results.

1. In the transplantation of a complex organ which performs a complex function, it would seem desirable not to interrupt the nutrition to the transplant while it is being manipulated and transferred. Most especially this principle would seem to be applicable in the case of the heart, which must continuously have the nourishment to be a dynamic pumping organ, or it dies as a pump and the organism that it serves succumbs. Therefore there must be an uninterrupted blood supply to the coronary arteries of the transplanted heart during the entire operation. This is accomplished by the perfusion of the coronary system by means of the blood of a third animal (interim parabiotic perfusion). This perfusion is not discontinued until the graft is nourished by appropriate vascular connection with its host. The third animal, known as the blood donor, supplies arterial blood from one of its carotid arteries to the coronary arteries of the heart to be transplanted; the coronary venous outflow is returned to one external jugular vein of the blood donor. Thus the heart is nourished and is beating at all times without interruption; it is a living organ at all times. This method we have called interim parabiotic perfusion; it is a homologous extracorporeal pump.

2. Whether or not the left heart is functioning, provision must be made for the right heart to be a functioning organ—this, in order that the coronary venous outflow via the coronary sinus into the right auricle be ejected and not accumulate to distend the right chambers.

3. Precaution against dilatation of the right heart must be taken, preferably by using one of the main pulmonary arteries as the outflow for the right ventricle.

5. Mann, F. C.; Priestley, J. T.; Markowitz, J., and Yater, W. M.: Transplantation of the Intact Mammalian Heart, Arch. Surg. **26**:219, 1933.

6. Sinitsyn, H.: Transplantation as New Method in Experimental Biology and Medicine, 1948, Moscow; photostat of dispatch No. 763 from Army Medical Library, Washington, D. C.

7. Marcus, E.; Wong, S. N. T., and Luisada, A. A.: Homologous Heart Grafts, read before the Surgical Forum of the 37th Clinical Congress, The American College of Surgeons, San Francisco, November, 1951.

8. Luisada, A. A.; Marcus, E., and Wong, S. N. T.: The Behavior of the Transplanted Heart, read before the Meeting of the American Heart Association, Cleveland, April, 1952.

4. Adverse reflexes producing arrhythmias of the transplant while it is being removed from the heart donor's body are best avoided by initial bilateral vagotomy in the neck.

5. Arterial air embolism must assiduously be guarded against. One little air bubble in the perfusion setup may cause fatal coronary artery air embolism, which cannot be overcome.

6. Intravascular thrombosis must be prevented. To strike just the right amount of anticoagulant to prevent thrombosis and yet not have serious bleeding of the wounds is very difficult. As in clinical vascular surgery, this problem remains unsolved.

7. The best heart graft is the heart of a young animal, preferably the heart of a puppy into the body of its mother.

The experiment requires the use of three dogs, the heart donor (preferably a puppy of 3 to 5 kg.); the blood donor, for the perfusion; and the heart recipient (preferably a large, healthy animal). All dogs are anesthetized with pentobarbital intraperitoneally, 35 mg. per kilogram of body weight, supplemented with ether as necessary. Occasionally the recipient was anesthetized with morphine followed by intravenous injections of thiopental (pentothal®) sodium. Aqueous heparin is administered to both the heart donor and the blood donor, the latter receiving a saline infusion containing additional heparin. The proximal ends of one carotid artery and one external jugular vein of the blood donor are cannulated, the cannulae and attached polyethylene tubing containing heparinized saline. The heart donor is now prepared. The neck is first entered; bilateral vagotomy is performed, and then a tracheostomy is made to an artificial respiration apparatus.[9] The chest of this animal is now opened, preferably by removing a front plate of the thoracic cage. The internal mammary arteries are immediately secured. If any arrhythmia is present, the heart and pericardium are treated with a solution of 2 to 4% cocaine or 2% procaine hydrochloride. One proceeds next to the dissection of the branches of the aorta. The tubing leading from the carotid artery of the blood donor is cannulated to the proximal end of the heart donor's left subclavian artery. The tubing leading to the blood donor's external jugular vein is similarly cannulated to the proximal end of one of the heart donor's cavae, usually the superior. The innominate artery is cleansed of branches from the arch to its trifurcation and isolated for later use. The azygos vein, the remaining cava, and the aorta are then rapidly freed, clamped, and ligated. As this is done, the clamps on the perfusion tubes are opened and the coronary blood flow of the heart transplant is now from the blood donor dog. This is the interim parabiotic perfusion. The inferior pulmonary ligaments, the mediastinal pleura, and the trachea are severed, care being exerted not to cut across intercostal and esophageal branches of the aorta. The entire heart-lung preparation is now transferred, with the heart beating regularly, to a basin of Ringer's solution at 38 C. The left main pulmonary artery is dissected free and saved for future use. Pneumonectomy is now accomplished. If heparinization of the blood donor and of the perfusion tubing is adequate, the detached heart can be kept beating indefinitely. The electric defibrillator and the drugs, epinephrine, calcium chloride, and procaine, should be at hand during the experiment.

In most cases, the recipient site in the recipient animal has already been prepared. The common iliac artery and vein, the common carotid artery and external jugular vein, and the femoral artery and vein, have alternatively been used in the experiments. The anastomoses of the vessels may be accomplished by suture technique (which is preferable), by double-end cannulae of glass, metal, or polyethylene, or by the intima-to-intima single-end cannulae, as used by Blakemore and others. Three different types of relationship between the circulation of the host and that of the heart transplant have been established.

In Group I only the right side of the heart is a functioning organ, with the host supplying arterial blood to the coronary arteries, but with an empty left ventricle. The right heart functions in that it ejects the coronary venous outflow. In this group the recipient's proximal artery is anastomosed to the innominate artery of the heart preparation and the aorta of the heart preparation to the distal artery of the recipient. The left main pulmonary artery of the heart preparation is anastomosed to the proximal end of the recipient's vein. In the early experiments, one or both cavae were joined to the proximal end or to both ends of the recipient's vein. This did not permit adequate outflow from the right heart unless an atrial septal defect

9. The M. S. A. Pneofore, (an artificial respiration apparatus) is manufactured by the Mine Safety Appliances Company, Pittsburgh 8.

was created, preferably by the method of Blalock and Hanlon.[10] With this atrial defect the left heart performs some work also. Use of the pulmonary artery as the outflow for the right heart is more natural and more desirable, for it prevents overdistention of the right side of the heart. As soon as the anastomoses are completed, they are opened; simultaneously, the interim parabiotic perfusion is discontinued. At this point the blood supply of the grafted heart is suddenly changed from that of the blood donor to that of the heart recipient (Fig. 1).

In Group II the left heart, as well as the right heart, is a functioning pump. Indeed, it supplies the power that fills its own coronary system. In this group the pulmonary artery to recipient proximal vein anastomosis is used for the right heart outflow just as in Group I. The inflow of arterial blood from the host, however, instead of splash feeding the grafted coronary system, is directed through the left auricle and ventricle. This is accomplished by joining the proximal artery of the host to either a large pulmonary vein or to the left auricular appendage. The blood courses through the auricle into the ventricle, from whence it is ejected

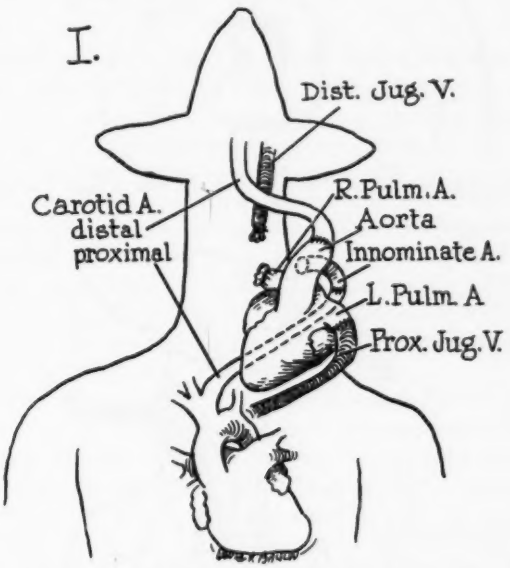

Fig. 1.—Relationship between circulation of host and that of heart transplant in Group I.

into its own aorta which is ligated beyond the arch and its branches. Ligature of the aorta permits rebound of blood against the aortic valves into the coronary arteries. Since the output of blood from the left ventricle is excessive for coronary flow alone, an outlet for the excess is provided by anastomosis of the innominate artery to the host's distal artery. That portion of the left heart output which is used by the grafted coronary system is returned via the coronary sinus to the right heart and thence via the pulmonary artery back to the host. This portion of the return constitutes an arteriovenous fistula (Fig. 2).

In both groups, if necessary to prevent kinking of the vessels, the heart preparation is anchored by a suture in the pericardium, near the apex, to the surrounding tissues. The recipient dog is heparinized with either aqueous or repository heparin, or both; occasionally, the anticoagulant therapy was started a day in advance of surgery, with ethyl biscoumacetate (tromexan® ethylacetate) administered orally. The wound is closed with provision for drainage by a small

10. Blalock, A., and Hanlon, C. R.: Interatrial Septal Defect—Its Experimental Production Under Direct Vision Without Interruption of the Circulation, Surg., Gynec. & Obst. **8:7**183, 1948.

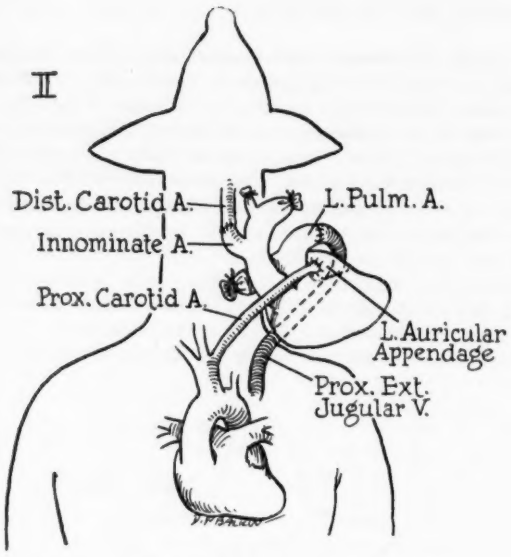

Fig. 2.—Relationship between circulation of host and that of heart transplant in Group II.

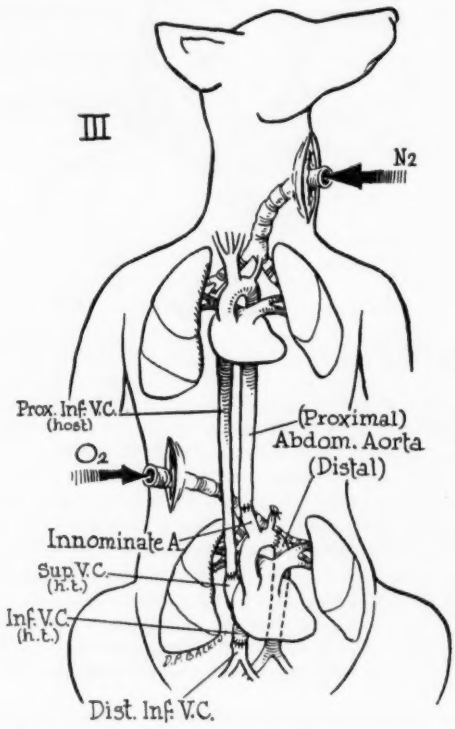

Fig. 3.—Relationship of circulation of host and that of heart transplant in Group III.

Penrose slip. Electrocardiographic and phonocardiographic records may now be made; pharmacologic experimentation may then follow, with simultaneous recording of the action of both hearts.

In Group III an attempt was made to transplant the heart with its own lesser circulation, the lungs. The purpose is to determine whether the heart and lungs as a pump-oxygenerator unit can deliver self-oxygenated blood to a delimited part of the host body. The heart-lung preparation was interposed either into the aorta-vena cava circulation just above their bifurcations or into the common iliac circulation. Blood was brought to the transplant from the host's cavae to the right auricle of the transplant, passed through its own lungs which were attached to an artificial respiration apparatus for oxygenation, and returned via pulmonary veins to the left heart which pumped blood out, supplying a part of the host's body and its own coronary arteries as well. This hypothesis was tested (1) by connecting the host's trachea to a source of nitrogen only, (2) by temporary ligature of the host's main pulmonary artery, providing an empty left auricle and ventricle, and (3) by occlusion of the tricuspid valve in an attempt to empty both sides of the host's heart (Fig. 3).

RESULTS

To date, 58 experiments have been carried out. In the first eight attempts, as the technique was being developed, no actual transplantation was accomplished.

The dog's heart was successfully transplanted into the circulation of another animal in Group-I fashion (right heart functioning) 15 times. In 13 of these 15, it was transplanted as a living pumping organ while being perfused with another animal's blood. In two others, it was transplanted after the cessation of all contractions, but the organ resumed its beating after a period of irregular contractions. One of these hearts had been washed in running tap water and had been still for 45 minutes; the anastomoses were completed for practice only. The resumption of rhythmic contractions for five minutes (before fibrillation due to coronary artery air embolism ensued) was an unexpected and startling experience. Maximum survival times were 45 and 48 hours (Table, A).

Transplantation in Group-II fashion (all four chambers functioning) has been accomplished 22 consecutive times without failure. Operating time has decreased, and, although average survival time has risen, maximal survival time has not yet risen above the 48-hour period. At the end of this period the transplanted heart and surrounding tissues exhibit a markedly angry-looking inflammatory edema not seen in wounds that contain no foreign protein. A histologic study of the transplanted heart and of the surrounding tissues after cessation of contractions is being made and will be reported at a later date (Table, B).

Eight heart and lung preparations have been transplanted (Group III). Attached to its own oxygenator, such a heart-lung transplant has lived for 75 minutes after the heart of the host animal had died. On one occasion, the heart beat and pumped oxygenated blood to a portion of the host's body for 61 minutes after the host's lungs were purple by virtue of inhalation of 100% nitrogen. On another occasion, the heart and lung preparation lived within the abdominal cavity of the recipient for over nine hours, during which time it was necessary to defibrillate it three times (Table, C).

On two occasions, after the heart and lung preparation was working in the aorta-vena cava circulation, the chest of the host was entered and the main pulmonary artery was temporarily completely occluded to empty the left side of the heart. The host's heart was then entered through a wide-open left atrial appendage, and manipulations of the mitral valve were made under direct vision. After seven minutes the

Homologous Transplant Series

Experiment No.	Date	Survival of Homologous Transplant	Comment
			A. Group I
9	4/ 9/51	5 min.	Ventricular fibrillation
10	5/16/51	45 min.	.....
11	5/23/51	5 min.	Air embolism of coronaries; heart washed in water
12	6/20/51	10 min.	Arrhythmias; no drugs available
13	6/27/51	2 hr.	.....
14	7/11/51	5½ hr.	Blalock interatrial defect; hemorrhage
15	7/25/51	Immediate	Heterologous transplant of cat into dog
16	8/ 1/51	45 hr.	Recipient dug out and ate homologous transplant; Blalock septal defect
17	8/ 8/51	6-14 hr.	Too small a branch of pulmonary artery was used; found thrombosed
20	8/29/51	7 hr.	Recipient died at 7 hr., too much anesthesia and postoperative fluids; pulmonary edema
21	9/ 5/51	7 hr.	Recipient died at 7 hr.; pulmonary edema
22	9/25/51	1 hr.	Entire system became thrombosed despite apparent adequate heparinization
23	10/17/51	7 hr.	Recipient died at 15 hr. of hemorrhage; had very low blood pressure entire 15 hr.
24	10/24/51	48 hr.	Homologous transplant was removed on the 7th postoperative day, was digested to less than one-half its size
25	10/31/51	Few min.	Uncontrollable right heart distention
51	6/11/52	29-41 hr.	Into common iliac circulation; preliminary splenectomy of host; lungs of heart donor had extensive pneumonitis
			B. Group II
26	11/21/51	.....	Pilot experiment; coronary air embolism
27	11/28/51	2 hr.	Persistent right heart distention; autopsy showed puppy heart to have no interatrial septum whatever
28	12/ 5/51	5-12 hr.	Air embolism of recipient's right heart; pulmonary edema
29	12/ 9/51	5 hr.	Recipient died at 5 hr.; hemorrhage from pulmonary vein anastomosis was troublesome from start; O_2 and digitalis slowed and strengthened homologous transplant beat, and it beat until recipient died
30	12/12/51	12-17 hr.	Recipient died between 12 and 17 hr.; hemorrhage from carotid-pulmonary vein anastomosis
31	12/19/51	Min.	Trouble with left heart outflow anastomosis; L. auricle blew out shortly after completion
32	1/ 2/52	<16 hr.	Knocked O_2 tank over on himself during night; some hemorrhage from L. heart outflow anastomosis
33	1/ 9/52	.....	Accidental destruction of L. subclavian artery. Heart and tubing placed in abdomen of blood donor; dog dead within 12 hr.—had donated too much blood
34	1/16/52	<17 hr.	Carotid to atrial appendage; slow bleeding at base of innominate artery; recipient died at 17 hr.
35	1/23/52	<14 hr.	Recipient died in somewhat less than 14 hr.; some hemorrhage at base of innominate artery
39	2/10/52	16 hr.	Recipient died at 16 hr.; no cause found
40	2/13/52	44 hr.	Heart transplant died suddenly at 44 hr.; reduced amount of heparin in this experiment; removal of heart at 52d hour showed reactive edema of homologous transplant and surrounding area; no gross disintegration; recipient continued to live
41	2/20/52	36 hr.	Recipient died at 68 hr.; autopsy done at 92 hr.; homologous transplant was edematous with reactive adhesive edema to tissues; no hemorrhage or distention; no cause for death of recipient found; no thromboembolism; small hemorrhages in loose anterior mediastinal tissues of recipient
42	2/24/52	2 hr. 40 min.	No hemorrhage at surgery; blew out pulmonary vein; sudden death of recipient
43	2/27/52	31-42 hr.	Autopsy of homologous transplant revealed 50 cc. of intrapericardial hemorrhage; antemortem clots in right ventricle and pulmonary artery; recipient survived
44	3/19/52	12-18 hr.	Heart recipient received 1,500 mg. cortisone over 36 hr. period including day of surgery; all dogs blood type AC; recipient was too deeply anesthetized; very lethargic postoperatively; examination of homologous transplant showed antemortem clots in all chambers; ? inefficient heparinization or ? of cortisone effect
45	3/26/52	Something under 42 hr.	Typical appearance of homologous transplant and tissues; heart chamber all right, but both arterial cannulae clotted; 1,250 mg. cortisone during 48 hr. prior to and on day of surgery

Homologous Transplant Series.—Continued

Experiment No.	Date	Survival of Homologous Transplant	Comment
48	5/ 7/52	20 hr.	Polyethylene cannulae; one little air bubble—probably coronary artery air embolism; procaine hydrochloride (pronestyl®) repeatedly necessary (3x) to restore normal rhythm; no thrombosis
49	5/21/52	21 hr.	Polyethylene cannulae; very fast technical procedure
50	6/ 4/52	40 hr.	Demonstration of coronary circulation of transplant with fluorescein, great difficulty of L. auricle adjusting to arterial pressure; inflow to left auricle from distal carotid of host; few bubbles of air in coronary arteries
			C. Group III
36	1/30/52	1 hr.	Lungs suffused with blood; M.S.A. pneofore not set high enough; difficulty with venous return
37	2/ 3/52	1 hr., 15 min.	Homologous transplant beat 75 min. after host's heart had died; host's trachea was clamped
38	2/ 6/52	1 hr., 25 min.	Homologous transplant beat 85 min. after hook-up; 61 min. after host's trachea was attached to N_2 tank (with host lungs purple), and 17 min. after host's heart had died
47	4/23/52	9 hr.	Ventricular fibrillation at 80 min.; successfully defibrillated; again successfully defibrillated at 3 hr. 45 min.; standstill at 5 hr. 15 min.; successfully restarted with compression and epinephrine; homologous transplant dead at 9 hr; much too much pentobarbital (nembutal®) intravenously to recipient
55	8/27/52	.....	L. auricle open 7 min. with pulmonary artery occluded
56	9/ 3/52	.....	Attempt to empty all chambers of heart by occlusion of tricuspid valve; ventricular fibrillation of host's heart after 10 min. of occlusion; homologous transplant functioning well
57	9/10/52	.....	Pulmonary artery occluded 15 min.; L. auricle appendage open 8 min.; homologous transplant functioned well and later removed; recipient in shock 1 hr. later
58	9/17/52	.....	Host's pulmonary artery occluded 16 min.; host's left auricle appendage open 7 min.; homologous transplant removed; chest closed and spontaneous breathing resumed; eye reflexes present at end of procedure

atrium was closed and then the appendage amputated. The pulmonary artery remained occluded once for 15 minutes and once for 48 minutes and then was released. Its coronary arteries, in the meantime, had been supplied with oxygenated blood from the heart-lung transplant in the abdomen.

Amongst the difficulties that must be avoided in the heart transplant is the disturbance of rhythm by reflex or mechanical causes. The former can usually be prevented by means of bilateral cervical vagotomy in the heart donor at the very beginning of the experiment and by effective cocainization of the heart when indicated. The latter is usually consequent upon varying degrees of overdistention of the right heart. Such overdistention may be caused by inadequate venous return to the blood donor due to kinking of a vein or intrapolyethylene tube thrombosis; another less appreciated cause is the tremendous increase in coronary artery flow and therefore in coronary venous return to the right auricle as a result of hypoxia from any cause. Maraist and Glenn [11] have shown that hypoxia may increase the coronary sinus outflow sixfold. Such overdistention can be largely prevented by using a main pulmonary artery as the right heart outflow tract anastomosed to the recipient's proximal vein. If this is not done, and the cavae used instead, an interatrial septal defect must be made at the outset. It was repeatedly observed that overdistention of the right heart rapidly led to various disturbances of rhythm and ultimately to

11. Maraist, F. B., and Glenn, W. W. L.: Coronary Blood Flow as Measured Directly with the Caval Venous Return Shunted Past the Right Heart, Surgery **31**:146, 1952.

ventricular fibrillation. Coronary artery air embolism spells quick and final defeat; it must assiduously be avoided. Anastomosis of a host artery to a transplant's pulmonary vein is fraught with danger because the dog's individual pulmonary vein is like the finest tissue paper; the smallest needle hole will permit hemorrhage when the pulmonary vein is subjected to a pressure to which it is totally unaccustomed.

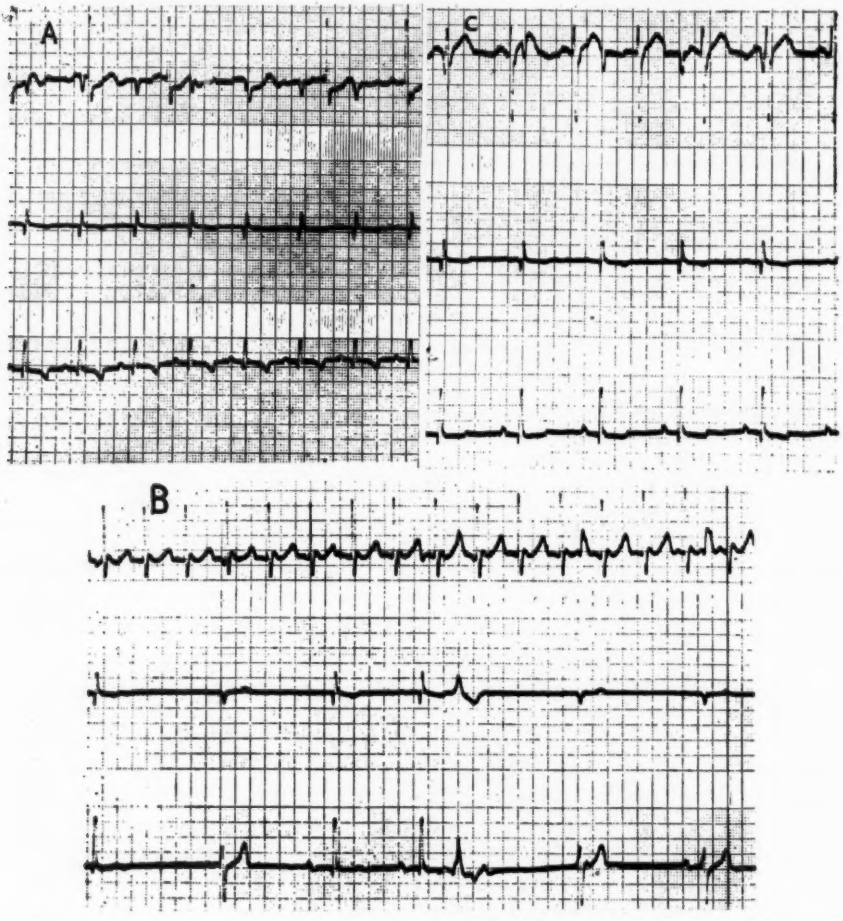

Fig. 4.—*A*, upper tracing, unipolar lead from neck of recipient, showing large complexes of transplanted heart (and small complexes for distant recipient's heart). *B*, same tracings as in *A*; upper tracing reveals a sinus tachycardia of transplanted heart following intravenous injection of 0.05 mg. of epinephrine (adrenalin®). The other two tracings reveal sinus arrest, sinus brachycardia, nodal escapes, and extrasystoles of recipient's heart. *C*, same tracings as in *A*, reestablishment of regular rhythm in animal's own heart; sinus rhythm with changed axis and voltage in transplanted heart.

Even when the host's artery is joined to the atrial appendage, the latter may at first balloon out and then adjust itself, only to have a pulmonary vein, ligated in the pneumonectomy, blow out.

Electrocardiograms and phonocardiograms have been obtained, demonstrating graphically the presence of two hearts within one body, usually with entirely separate and independent rates. Pharmacologic experimentation has begun to uncover some interesting findings. For example, the recipient's heart and the heart transplant, the

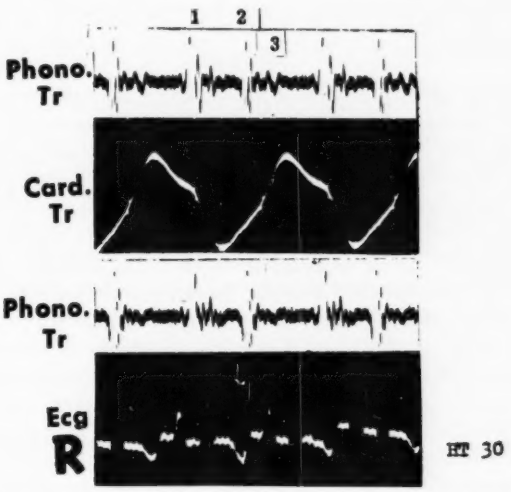

Fig. 5. —Upper tracings, phonocardiogram and volume tracing of transplanted heart (*Tr*); lower tracings, phonocardiogram of transplanted heart (*Tr*) and electrocardiogram of recipient heart (*R*).

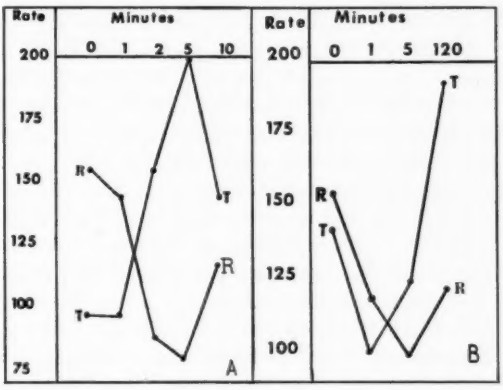

Fig. 6.—*A*, graphic analysis of diverging action of epinephrine on the two hearts. *B*, graphic analysis of action of digitalis on the two hearts.

latter devoid of nervous connections but bathed by the same blood as its host, react with different patterns to the drugs epinephrine and digitalis. The results of these studies have been briefly presented elsewhere [8] and will be reported in detail at a later date. Included in this report are some typical samples only. Figure 4 shows simultaneous electrocardiograms of the recipient's heart and of the heart transplant

through a unipolar lead from the neck: (*A*) base line record, (*B*) record immediately after the injection of epinephrine, and (*C*) record several minutes later. Figure 5 shows the simultaneous recording of the phonocardiogram of the heart transplant and the electrocardiogram of the recipient's heart. Figure 6*A* is a graphic analysis of the diverging action of epinephrine on the two hearts. Figure 6*B* is a graphic analysis of the action of digitalis on the two hearts.

COMMENT

Undoubtedly, the greatest deterrent to long survival of the transplanted heart is the biologic problem of tissue specificity involved in any homologous transplantation. Failure is due to some "strange biologic incompatibility" (Dempster [4]). The problem of homologous compatibility of tissue promises to be more difficult of solution than the compatibility of blood; the latter, to be sure, is also a tissue, but one that is more amenable to study than other tissues, with the means known to science today.

In order to prevent, as far as possible, tissue incompatibility, we have tried to work on a series of cross matched animals. Ninety per cent of mongrel dogs belong to one of two major blood groups (Hamilton [12]). Dempster reports that blood typing down to the M and N groups does not insure longer survival of homologous transplants. Many of the reactions between red cells and isoantibodies in transplants are analogous to those in humans (Young and co-workers [13]). In order to avoid these as far as possible, our dogs were studied according to the method of Young and his associates during the last six months of this work. In spite of this precaution, maximum survival time of the transplanted heart did not increase.

Several modalities have been suggested for depression of the host's fierce immunologic reaction to a homologous graft. Amongst them is suppression of the reticuloendothelial system by (1) total body irradiation (Murphy and Sturm [14]), (2) administration of corticotropin and cortisone (numerous, as reviewed by Dempster [4]), and (3) mechanical blocking (Saphir and Appel [15]). The last five recipients in Group II of this series have received cortisone, three of them probably in insufficient doses. Further immunologic developments are eagerly awaited.

Three sequelae may be expected to this type of experimental investigation. First, a transplanted heart would seem to be a most valuable test object for study of the physiologic and pharmacologic properties of the heart. The comparison of responses of the innervated (recipient's) and the denervated (transplanted) hearts within one body environment may shed further light on the function of this remarkable organ. Second, one may speculate that perhaps some day, when the problems of tissue specificity are solved, the transplanted heart may act as an accessory pump to a delimited region to decrease the work load of the central heart, even if only temporarily. Third, a transplanted heart or heart-lung preparation might be used for

12. Hamilton, A. S.: Study of in Vitro Methods for the Demonstration of Iso-Agglutination with the Bloods of Normal and of Ill Dogs, Am. J. Physiol. **154**:525, 1948.

13. Young, L. E.; O'Brien, W. A.; Miller, G.; Swisher, S. N.; Ervin, D. M.; Christian, R. M., and Yuile, C. L.: Erythrocyte-Isoantibody Reactions in Dogs, Tr. New York Acad. Sc. **13**:209, 1951.

14. Murphy, J. B., and Sturm, E.: Comparison of Effects of X-Ray and Dry Heat on Antibody Formation, J. Exper. Med. **41**:245, 1925.

15. Saphir, O., and Appel, M.: Attempts to Abrogate Immunity to Brown-Pearce Carcinoma, Cancer Res. **3**:767, 1943.

replacement of a diseased organ. The possibility of using a heterologous heart-lung preparation as an extracorporeal pump during intracardiac procedures is suggested. Others [16] have used the lungs only in an extracorporeal arrangement with a mechanical pump.

SUMMARY

The technique of interim parabiotic perfusion is described for the homologous transplantation of a heart in the dog. Important principles of the procedure are emphasized.

Such a transplanted heart becomes a valuable test object for the study of properties of the heart.

Results of transplantation of the heart in three different relationships to the recipient are presented.

The general biologic problems of the transplantation of a complex automatic organ and of tissue specificity in homologous transplants are touched upon.

Speculation is made on the ultimate use of a transplanted heart as a replacement functioning organ.

To satisfy clinical demands for the use of grafts in surgery, it will behoove surgeons to cooperate with geneticists and immunologists in the solution of problems basic to homologous transplantation.

25 E. Washington St. (Dr. Marcus)

ADDENDUM

Since this paper was submitted for publication we have obtained one six-day and one six and one-half-day survival of the transplanted heart in Group II. Interrupted everting mattress sutures were used, and less postoperative heparin was given in these experiments. These are the first instances in which hearts with all four chambers functioning have survived for such a long time. All previously reported transplants, made by ourselves and others, were similar to our Group I series or had shorter survival.

16. Fischer, H. W.; Albert, H.; Riker, W. L., and Potts, W. J.: Successful Experimental Maintenance of Life by Homologous Lungs and Mechanical Heart, Ann. Surg. **163**:475, 1952. Mustard and Chute, cited by Janes, R. M., in discussion on Fischer.

POSTGASTRECTOMY STRICTURE OF THE EFFERENT LOOP AND ITS TREATMENT

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NONFUNCTIONING or malfunctioning anastomosis after gastroenterostomy or subtotal gastric resection is a relatively frequent postoperative complication, which may or may not necessitate further surgical intervention. Eastman and Cole [1] encountered 7 cases of postoperative obstruction in a series of 191 gastrectomies. In a series of 100 cases reported by Gray and Sharpe [2] in which posterior gastroenterostomy had been performed for duodenal ulcer, the incidence of gastric retention was 35%. Certain changes in the technique of operation and of postoperative care reduced this complication in another series of 100 cases to 19%. Serious retention was recorded in 24% in the first series and in 13% in the second group.

A multitude of factors may be responsible for postoperative gastric retention. According to location, they may be divided into three groups:

1. Those affecting the proximal or afferent limb. When the resection has been unusually high, a kink may form where the afferent loop joins the lesser curvature of the stomach.[3] The long jejunal loop in the antecolic anastomosis may cause filling of the afferent limb, which may obstruct the stoma. Kinking of the duodenojejunal angle may produce a similar result.[2]

2. Stomal changes. A spur at the anastomotic site, produced by the festooning descent of the afferent and efferent jejunal limbs, may cause obstruction. Herniation of the anastomosis, which may occur when the edges of the mesocolon have not been properly anchored to the stump of the stomach, is likely to cause angulation of the retracted jejunum. Inverting excessive amounts of tissue in the performance of anastomosis is likely to create a constricting ring within the stoma. Nonfunction of the stoma may be due to the edema, attributable to hypoproteinemia,

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1. Eastman, W. H., and Cole, W. H.: Precautions and Results in Gastrectomy, Arch. Surg. **59**:768, 1949.

2. Gray, H. K., and Sharpe, S. W.: Gastric Retention After Postoperative Gastro-Enterostomy for Duodenal Ulcer: Prevention and Treatment, Ann. Surg. **123**:397, 1946.

3. Wangensteen, O. H.: Aseptic Resections in the Gastro-Intestinal Tract with Special Reference to Resection of Stomach and Colon, Surg., Gynec. & Obst. **72**:257, 1941.

as demonstrated by Barden, Ravdin, and Frazier.[4] Edema of the stomal site may also be associated with traumatic inflammatory gastrojejunitis.

3. Those affecting the distal or efferent limb. Kinking or twisting of the distal limb of the jejunum as it leaves the gastric wall in an isoperistaltic anastomosis may produce obstruction. As Wangensteen [3] pointed out, a likely cause of obstruction of the efferent outlet is its narrowing in antiperistaltic anastomosis made according to the Billroth II or Hofmeister plan, if the surgeon inverts more of the readily available jejunum than he should. Pressure on the jejunal loop by the middle colic artery, if the anastomosis is made to the right of the artery, may also represent a causative factor in creation of an obstruction. Newly formed adhesions between the efferent loop and adjoining tissues may lead to a stricture.

No completeness is claimed for this brief review of conditions which may play a role in gastric retention. In many instances a combination of several factors may be responsible for malfunctioning of the gastric stoma.

This discussion is limited to the choice of procedures designated to relieve obstruction of the efferent limb.

If conservative measures, such as decompression and correction of hypoproteinemia, fail, exploration is indicated.

A kink or twist of the jejunum close to the stoma in isoperistaltic anastomosis usually can be corrected by isolating the involved segment and placing it in proper position.

If in antiperistaltic anastomosis too much tissue has been inverted, the constricting ring must be excised and gastrointestinal continuity restored by creation of a new anastomosis.

If the surgeon feels that the condition is of an inflammatory character, jejunostomy may be considered. This operation permits feeding an adequate diet while the involved area is put at rest, thus allowing the inflammatory process to subside. The disadvantage of this procedure lies in the risk that, should the obstruction not subside, a third intervention may become necessary.

If the adhesions are found between the efferent limb and the adjoining tissues, the first thought, of course, is directed to an attempt to free the adherent segment. However, firm adhesions between the jejunum and vital organs, such as the pancreas, may create insurmountable technical difficulties.

If only a short stump of the stomach remains after an extensive gastrectomy, a second gastroenterostomy is technically impossible.

A sidetracking operation, in the form of Braun's anastomosis, between the afferent and the efferent limbs, below the stenosis, may come into consideration. However, great technical difficulties may be encountered if the proximal loop is very short or is adherent to the adjoining tissues. In such cases the establishment of an anastomosis between the stomal portion of the jejunum and the jejunal segment below the stricture may solve the problem. The difference between this procedure and Braun's anastomosis lies in the fact that in the former procedure not the afferent limb but the stomal portion of the jejunum is used for the new anastomosis.

4. Barden, R. P.; Ravdin, I. S., and Frazier, W. D.: Hypoproteinemia as a Factor in the Retardation of Gastric Emptying After Operations of the Billroth I or II Types, Am. J. Roentgenol. **38**:196, 1937.

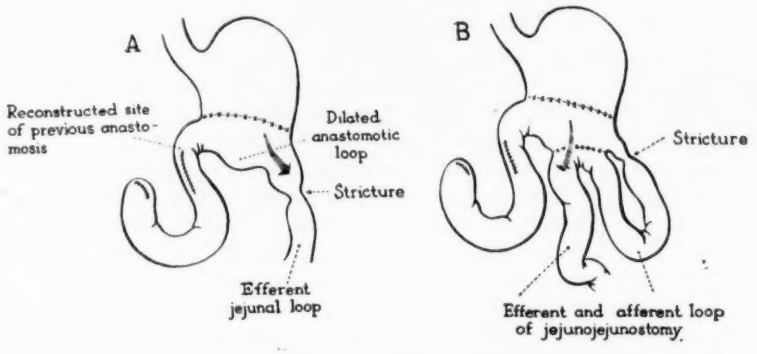

Fig. 1.—*A*, anastomotic portion of jejunum is greatly dilated, while efferent loop is constricted 4 cm. below stoma by adhesions to denuded area of pancreas. *B*, establishment of new communication between anastomotic loop of jejunum and its segment located below stricture.

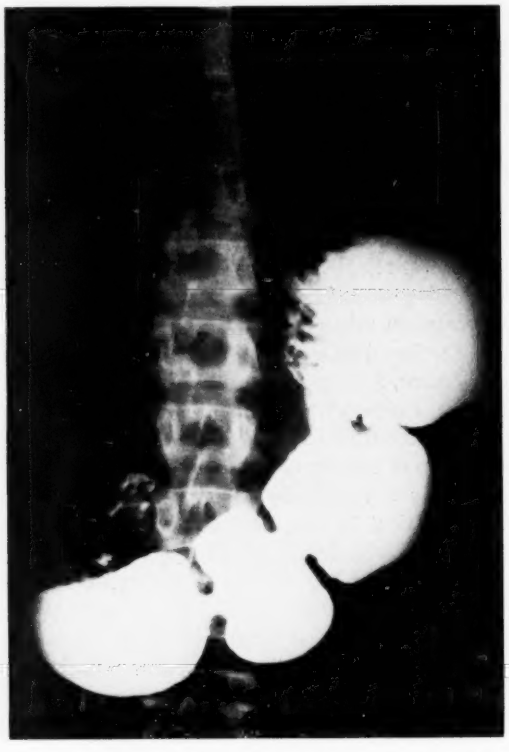

Fig. 2.—Roentgenogram illustrating condition before gastroenterostomy—hyperstalsis and duodenal ulcer but no evidence of stomach ulcer.

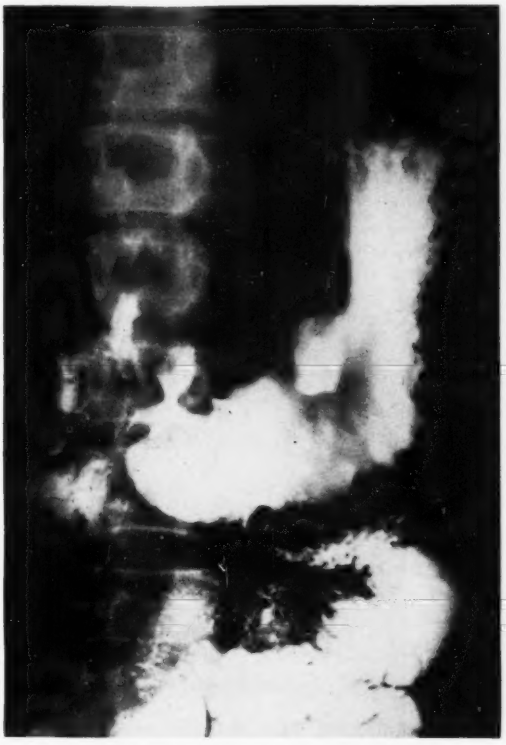

Fig. 3.—Roentgenogram illustrating condition two and one-half years after gastroenterostomy—well-functioning gastroenterostomy; duodenal ulcerations and nonmarginal perforated ulcer on the lesser curvature, with so-called accessory pocket.

Fig. 4.—Photograph of gross specimen removed by gastric resection. Removed specimen has been incised along greater curvature and opened like an oyster shell. Lower arrow points to site of gastroenterostomy; upper arrow, to ulcer on lesser curvature, with crater leading to accessory pocket.

REPORT OF A CASE

The following case illustrates the employment of the method described above.

A man 38 years of age remained asymptomatic for a period of two and one-half years after posterior gastroenterostomy was performed for a duodenal ulcer. An examination, done because of recurrence of pain and vomiting, disclosed a well-functioning stoma, a duodenal ulcer, and a large gastric ulcer, which perforated and was walled off by a large pocket.

The operation confirmed the roentgenologic findings. In addition to a duodenal ulcer there was a very large saddle ulcer in the midportion of the lesser curvature, which had formed a pocket within the pancreas.

Fig. 5.—Photograph of saddle ulcer on lesser curvature, with crater in its center. Lower half of picture represents posterior stomach wall and upper half, anterior wall; actual size.

The anastomosis was disconnected, and the normal continuity of the intestinal tract was reestablished by transverse closure of the rent in the jejunum. After the ulcer crater was dissected from the pancreas, a retrocolic gastric resection according to the Polya-Balfour method was performed.

Four days after the operation, symptoms of an acute obstruction developed. Since all conservative measures failed and the patient's condition became critical, an exploratory laparotomy was performed seven days after the gastric resection. The anastomotic portion of the jejunum was greatly dilated (Fig. 1*A*), while the efferent loop was constricted 4 cm. below the stoma by adhesions to the denuded area of the pancreas. It was evident that isolation of the constricted segment could not be accomplished without much trauma to the pancreas and that the involved section of the bowel would not remain patulous. Since the proximal limb of the jejunum was adherent to the pancreas, a new communication was established between the anas-

tomotic loop of the jejunum and its segment located below the stricture (Fig. 1*B*). After this operation the patient made an uneventful recovery and has gained weight. At the follow-up examination 13 months later there was no evidence of a dumping syndrome or of a marginal ulcer.

COMMENT

Millbourn,[5] Warren,[6] Lahey,[7] and many others have warned of the hazards of pancreatitis following removal of peptic ulcers from the pancreas. They urge avoidance of the introduction of needles or sutures into the pancreas, of laceration of the pancreatic ducts, and of constriction of the blood vessels. Heeding these warnings, after the stomach ulcer was dissected from the pancreas in the case reported above, no attempt was made to cover the affected surface. While damage to the pancreas was thus avoided, the large exposed area of this organ became adherent to the adjacent afferent limb and also to the efferent jejunal loop, causing a cicatricial stenosis in the latter. In such cases the unconventional employment of the stomal loop for the sidetracking jejunojejunostomy appears to be followed by good results.

SUMMARY

Various methods of treatment of postgastrectomy strictures of the efferent loop are discussed.

In cases in which, after gastrectomy, adhesions to the pancreas involve both the afferent and efferent limbs and cause a stricture of the distal loop, anastomosis between the stomal segment of the jejunum and the efferent loop below the anastomosis appears to be a suitable procedure.

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5. Millbourn, E.: On Acute Pancreatic Affections Following Gastric Resection for Ulcer or Cancer and the Possibilities of Avoiding Them, Acta chir. scandinav. **98**:1, 1949.

6. Warren, K. W.: Acute Pancreatitis and Pancreatic Injuries Following Subtotal Gastrectomy, Surgery **29**:643, 1951.

7. Lahey, F. H., and Marshall, S. F.: The Surgical Treatment of Peptic Ulcer, New England J. Med. **246**:115, 1952.

CANCER OF THE COLON AND RECTUM

Analysis of Eighty Cases

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IN THE presentation of such a broad topic as carcinoma of the colon, it is impossible to review all of the available literature on this subject. In the analysis of our cases, we will attempt to present data which will lay stress upon many important factors recently reported in the literature.

The cases included in this analysis consist of 80 in which operation was performed at this hospital during the past six years.

AGE INCIDENCE AND LOCATION OF LESIONS

The age incidence varied from 21 to 85 years, the average age of patients being 49.5 years. The average age of patients in the group without lesions of the appendix was 52.4 years. In the youngest group of patients, those with carcinoid of the appendix, the average age was 26.3 years. In this series of patients with cancer involving the various segments of the colon, 55% were in the sixth decade; 13% in the seventh decade, and 10% in the third decade. The age incidence and location of the lesions are shown in Table 1. This corresponds with the reports in the literature that the highest age incidence is in patients in the 50- to 65-year age groups, as shown by Bacon, Pennington, and Thomas.[1] As to location of the lesions in this series, the greater number are found in the rectum, rectosigmoid, sigmoid, and cecum. This was also found in the series reported by Boehme and Hanson,[2] Vynalek

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1. Fronduti, L. J.: Surgical Management of Tumors of the Right Half of the Colon, Surgical Staff Meetings Bulletin, Veterans Administration Hospital, Des Moines, Ia., 1948, Vol. 2, No. 7. Westly, G. T.: Surgical Treatment of Tumors of the Left Half of the Colon, Surgical Staff Meetings Bulletin, Veterans Administration Hospital, Des Moines, Iowa, 1949, Vol. 2, No. 8.

2. Boehme, E. J., and Hanson, P. J.: Carcinoma of the Colon and Rectum: Site of Growth of 1,457 Lesions, S. Clin. North America **26**:551, 1946.

and co-workers,[3] Mayo and Schlicke,[4] and Bacon.[5] In over two-thirds of their cases the lesions were present in the left half of the colon. The rectum showed the highest incidence, varying from 24.9% in Mayo's series [6] to 56.1% in Bacon's [5] series.

SYMPTOMS IN RELATION TO LOCATION OF LESION

The sequence of symptoms in carcinoma of the colon are variable, depending upon several factors, such as location, type, size, and associated complications. Generally, the onset is insidious. However, the first indications in many cases may be an acute bowel obstruction or perforation.

The duration of symptoms in this series was quite variable, ranging from a few days to 7 years, with an average of 10.4 months. This finding was comparable to that reported by Swinton and Gillespie [7] of 9 months, by Sherman [8] of 10.4 months, by Bacon [9] of 9.75 months, and by Thomas and co-workers [10] of 10.5 months. The longest duration of symptoms was associated with lesions involving the cecum, ascending colon, and sigmoid. The existence of symptoms in cancer of the left half

TABLE 1.—*Average Age Incidence According to Location of Lesion*

Location of Lesion	Per Cent	of Patient, Yr. Average Age
Rectum	28.75	53.3
Rectosigmoid	15.0	50.7
Sigmoid	12.5	52.4
Descending colon	2.5	52.5
Splenic flexure	6.25	47.4
Transverse colon	8.75	54.4
Ascending colon	6.25	55.2
Cecum	16.25	53.3
Appendix	3.75	26.3

of the colon was about the same as in cancer of the right half; the duration of symptoms prior to definitive surgery was over 400 days.

The over-all evaluation of frequency of symptoms and complaints for lesions in the various segments of the colon revealed that pain and change in bowel habits occurred most frequently, being present in 81.25% and 72.55%, respectively. Pain was more frequent in lesions involving the sigmoid and ascending and descending

3. Vynalek, W. J.; Saylor, L. L., and Schrek, R.: Carcinoma of Colon: Statistical Analysis, Surg., Gynec. & Obst. **84**:669, 1947.

4. Mayo, C. W., and Schlicke, C. P.: Carcinoma of the Colon and Rectum: Study of Metastasis and Recurrences, Surg., Gynec. & Obst. **74**:83, 1942.

5. Bacon, H. E.: Evolution of Sphincter Muscle Preservation and Re-Establishment of Continuity in the Operative Treatment of Rectal and Sigmoidal Cancer, Surg., Gynec. & Obst. **81**:113, 1945.

6. Mayo, C. W.: Surgical Procedures for Carcinoma of the Rectum and Rectosigmoid, J. Michigan M. Soc. **45**:1474, 1946.

7. Swinton, N. W., and Gillespie, J. L.: The Diagnosis of Carcinoma of the Colon and Rectum, S. Clin. North America **26**:553, 1946.

8. Sherman, L. F.: Carcinoma of the Colon and Rectum, Surgical Staff Seminars, Veterans Administration Hospital, Minneapolis, Minn., 1948, Vol. 4, p. 132.

9. Bacon, H. E.: Anus, Rectum, and Sigmoid Colon: Diagnosis and Treatment, Philadelphia, J. B. Lippincott Company, 1938.

10. Thomas, R. A.; Kline, P. S., and Seed, L.: Carcinoma of Rectum and Rectosigmoid: Statistical Analysis of 844 Cases, Arch. Surg. **56**:92, 1948.

colon. The highest incidence of change in bowel habits occurred most frequently in rectosigmoid, sigmoid, rectum, and splenic flexure lesions.

Weight loss occurred in 66.25% of patients, being commonest and greater in degree in patients with lesions involving the right half and the transverse colon, as compared with those with lesions in lower left half of the colon.

Blood in the stools or rectal bleeding developed in 48.75% of the patients, commonest in the rectosigmoid and sigmoid lesions and occurring in 78% of these lesions. This finding and complaint was present in 61.1% of the patients with lesions of the left colon, as compared with 26.5% of patients with lesions of the right colon. Of the right colon lesions, those involving the ascending portion were responsible for anemia and/or blood in the stool in a higher percentage of cases.

Fatigability, which developed in over 40% of the patients, was more prevalent and pronounced in the right-sided lesions, the highest percentage being in lesions involving the cecum.

Obstructing symptoms or findings were present in only 25% of the total cases. This finding occurred in 80% of the lesions of the splenic flexure, in 60% of the lesions in the ascending colon, in 50% of the lesions in the descending colon, and in 33% of the lesions in the rectosigmoid region.

The frequency of these symptoms as a result of lesions in the various locations in the colon compares similarly with the percentages reported by Coller and Berry,[11] Jones and co-workers,[12] Thomas and co-workers,[10] Johnson,[13] Sherman[8] and Rhoads.[14]

DIAGNOSTIC PROCEDURES

The presence of an abdominal mass or lesion was established by palpation in 35.2% of the total group of patients and in 60.2% of the patients with lesions involving the right colon. By rectal digital examination, a mass was palpated in 69.3% of the patients with lesions of the rectum, rectosigmoid, and sigmoid. Of these palpable lesions, 41% were in the rectosigmoid or sigmoid. In 91.3% of rectal lesions, the mass was readily palpable by digital examination. On proctoscopic examination, the mass or lesion was discernible in 100% of the patients with lesions of the rectum and rectosigmoid; whereas, 60% of the lesions of the sigmoid were reached with the sigmoidoscope.

The roentgenographic studies of the colon were positive in 90.7% of the patients; in the remaining number, the lesion was not visualized. Of the nonvisualized lesions, two were in the rectum, one at the rectosigmoid junction, and two in the sigmoid. The x-ray studies of the left half of the colon were positive in 89% of the cases, as compared with 94.4% in cases of right colonic lesions.

The value of all these methods in establishing the presence of a tumor is readily apparent; the higher the lesion is in the left half of the colon, the more accurate are the roentgenographic examinations; whereas, the lower the lesion, the more accurate are digital and proctoscopic examinations.

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11. Coller, F. A., and Berry, R. E. L.: Cancer of the Colon, J. A. M. A. **135**:1061, 1947.

12. Jones, T. E.; Robinson, J. R., and Meads, G. B.: One Hundred and Thirty-Seven Consecutive Combined Abdominoperineal Resections Without Mortality, Arch. Surg. **56**:109, 1948.

13. Johnson, T. M.: Carcinoma of the Rectum: Review of 215 Cases, J. Kansas M. Soc. **48**:62, 1947.

14. Rhoads, J. E.: Malignancy of the Colon and Rectum, Veterans Admin. Tech. Bull., TB 10-82, Feb., 1952.

In lesions involving the rectum and rectosigmoid, by rectal and proctoscopic examinations lesions were seen and/or palpated in 94% of the cases, as compared with 75% reported by Mayo,[15] 87% by Jones,[12] 70% by Jackman and co-workers,[16] 91% by Johnson,[13] and 70% by Swinton and his associates.[7] A mass was palpable abdominally in 16% of the group of patients with tumors of the left colon reported on by Cole.[17] The tumors were palpable in 21% of cases in our series. In right colonic lesions, a mass was palpable abdominally in 10% of the cases reported by Rankin,[18] as compared with 61% in our series.

TYPES OF LESIONS

Adenocarcinoma occurred in 95% of the patients, carcinoid in 3.75%, and epidermoid carcinoma in 1.25%. The latter lesion occurs infrequently; Cattell[19] reported 10 cases and Sweet[20] 77. In four, or 5%, of the patients, two separate lesions were found in the colon. In all these cases, the two lesions were both adenocarcinoma. In three cases, the lesions were in the right half of the colon, and in one

TABLE 2.—*Gross Appearance and Location of Lesion*

	Site and Number									
Type	Rectum	Recto-sigmoid	Sigmoid	Descending Colon	Splenic Flexure	Transverse Colon	Ascending Colon	Cecum	Appendix	Total
Fungating	13	2	2	..	..	2	4	10	..	33
Annular	5	3	2	1	5	2	1	..	..	19
Fungating annular	3	7	..	..	..	2	..	..	..	12
Polypoid	1	..	3	..	..	..	..	..	..	4
Carcinoid	..	..	..	..	..	..	..	..	3	3
Mucoid	..	..	..	..	..	..	..	2	..	2
Epidermoid	1	..	..	..	..	..	..	..	..	1
Unclassified	..	..	3	1	..	1	..	1	..	6
Totals	23	12	10	2	5	7	5	13	3	80

case, in the lower left half of the colon. The epidermoid carcinoma occurred in the lower anal canal, and in the three cases of carcinoid the appendix was involved.

Polyps were present in the colon in 17.5% of the patients in this series. The greatest number of polyps were found in the descending colon, sigmoid, and rectum.

The gross appearance of the tumors in this series and their location are tabulated (Table 2). The commonest type was a fungating tumor, occurring in 42% of the cases; an annular type of tumor occurred in 24%, a fungating-annular type in 15%, and a polypoid type in 5%.

In 31 (38.7%) of the patients, the tumor of the colon involved contiguous tissues or organs by neoplastic invasion or by inflammatory reaction. This involvement occurred in 34.6% of the lesions of the left half of the colon, as compared with 46.4% of the right half.

15. Mayo.[4] Mayo.[6]

16. Jackman, R. J.; Neibling, H. A., and Waugh, J. M.: Carcinoma of the Large Intestine: Diagnostic Errors in Relation to Location of Lesion, J. A. M. A. **134**:1287, 1947.

17. Cole, W. H.: Carcinoma of the Colon, Illinois M. J. **91**:229, 1947.

18. Rankin, F. W.: Principles of Surgery of the Colon, Surg., Gynec. & Obst. **72**:332, 1941.

19. Cattell, R. B., and Williams, A. C.: Epidermoid Carcinoma of the Anus and Rectum, Arch. Surg. **46**:336, 1943.

20. Sweet, R. H.: Results of Treatment of Epidermoid Carcinoma of the Anus and Rectum, Surg., Gynec. & Obst. **84**:967, 1947.

OPERABILITY

Of the 80 patients operated upon, in 47 (58.7%) the lesion was considered operable, and a definitive procedure was accomplished, whereas in 32 (40%) the lesion was considered inoperable, and in this group a palliative procedure was performed. In one patient, an exploration alone was carried out. For 70% of the lesions of the rectum, a curative type procedure was performed; 60% of the lesions involving the cecum or sigmoid were considered operable. Lesions involving the rectum, rectosigmoid, and/or sigmoid were operable in 66.6% of the cases. However, only 55% of the carcinomas of the cecum and ascending colon were operable. Cancer involving the transverse colon was inoperable in 71% of the cases.

Stone and McLanahan [21] reported an operability of 77% in their series of 191 cases of left colon lesions. Lahey's [22] operability rate was 83%, Allen's,[23] 95% in 105 cases. Ochsner's [24] resectability rate was 65% in 42 cases. Ravdin and his associates [25] in a series of 53 colon resections, reported a 73.6% resectability rate.

CAUSES OF DEATHS

Five (6.25%) deaths occurred during the immediate postoperative period; three following operations for lesions of the rectum and rectosigmoid, one for a lesion of the splenic flexure, and one for a lesion of the ascending colon. Four (5%) of the deaths were classified as surgical deaths. One occurred in a man in his eighth decade, who died on the 10th postoperative day of multiple kidney abscesses, pelvic abscess, and metastases in the lungs and mediastinal nodes; one patient in his fifth decade died on the 31st postoperative day of a lower nephron nephrosis and renal and cardiac failure; one patient in the fifth decade died on the 11th postoperative day of generalized peritonitis due to perforation at the site of the anastomosis; and the fourth patient in the fifth decade died on the 14th postoperative day of generalized carcinomatosis. The fifth patient died on the 18th postoperative day as a result of a ruptured esophageal varix; his death was not considered as a surgical death.

The postoperative mortality was 2.5% for patients with lesions of the colon which were considered operable; the same number of deaths, two (6.2%), occurred in those patients upon whom a palliative procedure was performed.

The mortality varies considerably in different localities in this country and also according to the time (1920 to 1940; 1941 to 1952) the procedure was performed. During the past several years the postoperative mortality has been lowered a great deal. In 1942 Lahey [26] reported a mortality of 11.7% for right colectomy; at the same time Stone and McLanahan [21] reported 19.8% mortality in a group in which

21. Stone, H. B., and McLanahan, S.: Resection and Immediate Aseptic Anastomosis for Carcinoma of the Colon, J. A. M. A. **120**:1362, 1942.

22. Lahey, F. H.: A Discussion of the Modified Mikulicz Operation for Carcinoma of the Colon and Its Technic, S. Clin. North America **26**:610, 1946.

23. Allen, A. W.; Welch, C. E., and Donaldson, G. A.: Carcinoma of the Colon: Effect of Recent Advances on Surgical Management, Ann. Surg. **126**:19, 1947.

24. Ochsner, A., and Hines, M. O.: Carcinoma of the Colon: Analysis of 113 Cases, South. Surgeon **12**:269, 1946.

25. Ravdin, I. S.; Zintel, H. A., and Bender, D. H.: Adjuvants to Surgical Therapy in Large Bowel Malignancy, Ann. Surg. **126**:439, 1947.

26. Lahey, F. H., and Sanderson, E.: Lesions of the Right Colon Involving Right Colectomy, J. A. M. A. **120**:1356, 1942.

an aseptic anastomosis was performed. In 1947 Mayo [27] reported a mortality of 3.8, while Cattell and his associates [28] had no deaths in 13 cases of primary resection of the right colon.

The mortality rates for lesions involving the left colon also show a decrease during the past several years. Gibbon and Hodge [29] in 1941 had a mortality rate of 28% in 72 open primary anastomoses and 14% in 246 closed anastomoses. Stone and McLanahan [21] in 1942 in 104 primary end-to-end anastomoses reported a 10.6% mortality rate. Allen and co-workers [23] reported a 2% mortality in open anastomosis in 105 cases. Ochsner [24] in 42 cases had a mortality of 6.6%. Ravdin [25] in 1946 reported 53 one-stage primary anastomoses, of which 18 were of the open type, with a mortality rate of 3.8%.

Coller and co-workers [30] prefer a primary end-to-end anastomosis. In a series of 209 curative resections the mortality rate was 1.9%. Hoxworth and Mithoefer [31] perform a primary end-to-end anastomosis for lesions of the left half of the colon. In 63 cases of primary anastomosis, the mortality rate was 7.9%.

In lesions of the left half of the colon and the upper sigmoid, Waugh and Chester,[32] with use of a primary anastomosis in 74 cases, reported a 5.1% mortality rate. In 67 cases of lesions of the left colon, with a primary anastomosis without decompression, McKittrick [33] had a mortality rate of 5.9%. Meyer and co-workers [34] in 52 cases of primary open anastomosis had 1 death.

In 137 resections of the colon with primary aseptic anastomosis the mortality rate was 5% in Wangensteen's [35] series. McNealy [36] reported two deaths (5.8%) in a group of patients with 34 bowel resections with a primary open anastomosis.

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27. Mayo, C. W.: Malignant Lesions of the Right Colon, with Particular Reference to One-Stage Resection, Postgrad. Med. **1**:430, 1947.

28. Cattell, R. B., and Colcock, B. P.: Primary Resection of the Right Colon, S. Clin. North America **26**:606, 1946.

29. Gibbon, J. H., Jr., and Hodge, C. C.: Aseptic, Immediate Anastomosis Following Resection of the Colon for Carcinoma, Ann. Surg. **114**:635, 1941.

30. Coller, F. A., and Vaughan, H. H.: Treatment of Carcinoma of the Colon, Ann. Surg. **121**:395, 1945. Coller.[11]

31. Hoxworth, P. I., and Mithoefer, J.: Management of Cancer of the Colon, Surgery **22**:271, 1947.

32. Waugh, J. M., and Custer, M. D., Jr.: Resection and Primary Anastomosis for Lesions of the Left Portion of the Colon, Postgrad. Med. **3**:85, 1948.

33. McKittrick, L. S.: Principles Old and New of Resection of the Colon for Carcinoma, Surg., Gynec. & Obst. **87**:15, 1948.

34. Meyer, K. A.; Sheridan, A., and Kozoll, D. D.: One Stage "Open" Resection of Lesions of the Left Colon Without Complementary Colostomy, Surg., Gynec. & Obst. **81**:507, 1945. Meyer, K. A., and Kozoll, D. D.: One-Stage Resection of Left Colon Lesions Without Colostomy, J. Indiana M. A. **40**:521, 1947.

35. Wangensteen, O. H.: Symposium on Surgical Management of Malignancy of Colon: Primary Resection (Closed Anastomosis) of the Colon and Rectosigmoid Including Description of Abdomino-Anal Methods for Restoration of Continuity Accompanying Excision of Carcinoma of Rectal Ampulla, Surgery **14**:403, 1943; Primary Resection (Closed Anastomosis) of Rectal Ampulla for Malignancy with Preservation of Sphincteric Function Together with Further Account of Primary Resection of Colon and Rectosigmoid and Note on Excision of Hepatic Metastases, Surg., Gynec. & Obst. **81**:1, 1945.

36. McNealy, R. W., and Lands, V. G.: Primary Anastomosis in the Treatment of Carcinoma of the Colon, Surgery **21**:283, 1947.

Cole [17] prefers a one-stage procedure in which obstruction is not present. In 50 cases of primary anastomosis he reported a 10% mortality rate. Hinton and Localio,[37] in 50 cases of primary anastomosis, one-stage, nonobstructive cases, had a mortality rate of 2%.

TYPES OF OPERATION

In practically all the cases an open method of intestinal anastomosis was accomplished as a one-stage procedure without a preliminary decompression colostomy. A temporary transverse colostomy was employed only in those patients (8%) with complete bowel obstruction. An end-to-end anastomosis was the procedure of choice for both right and left colonic lesions. An end-to-side ileotransverse colostomy was performed in the first group of right colonic lesions. However, during the past four years the end-to-end anastomosis has been utilized exclusively.

For lesions involving the sigmoid, rectosigmoid, and upper rectum, an anterior resection was carried out. In the majority of instances the lower limit of the tumor was 10 cm. above the anal verge. In several cases in the early group, anterior resection was performed for lesions at the 7- or 8-cm. level. In the past several years, however, the anterior resection has been limited to lesions at or above the peritoneal reflection.

In cases of low-lying rectal and anal lesions, Miles's abdominoperineal resection was performed. In three instances a pull-through operation was accomplished, and in two a posterior resection was performed.

Abdominal Incisions.—In all cases a muscle-splitting transverse or oblique abdominal incision was employed. For lesions of the right colon, the incision was made in a transverse direction at the level of the umbilicus and to the right of the lateral border of the rectus abdominis muscle. The underlying muscles of the abdominal wall were split in the direction of their fibers. For lesions of the left lower colon and rectum, a left oblique suprainguinal incision was made, splitting the muscles of the anterior abdominal wall, and in many cases extended to the midline with transection of the left anterior rectus sheath and rectus abdominis muscle. For lesions involving the splenic flexure, a left subcostal muscle-splitting incision was employed. For lesions of the transverse colon, a transverse supraumbilical incision was performed, transecting the anterior and posterior rectus sheaths and the rectus abdominis muscles.

The closure of these incisions was accomplished in layers, using nonabsorbable surgical (silk) sutures in 63 (78.7%) cases, fine wire sutures in 12 (15%), and absorbable surgical (gut) sutures in 5 (6.3%). There were no postoperative hernias in this group. In one patient (1.2%), a 71-year-old man, who had an abdominal-perineal resection, a wound infection developed, followed by a dehiscence on the 10th postoperative day.

Seven (8.7%) wound infections occurred, two in the group with left colonic lesions and five in the group with cecal or ascending colonic tumors. A wound hematoma developed in four (5%) cases, one in a left lower abdominal wound and three in the right midabdominal wound.

POSTOPERATIVE COMPLICATIONS

Forty-seven complications (including those of the wound) developed in 37 patients. A greater number of complications occurred in those patients with a right-sided lesion than in those with a left-sided lesion. Pulmonary complications were infrequent, occurring as atelectasis, pulmonary infarction, and hydrothorax, singly in three patients. The most frequent complication was bowel obstruction, which occurred in eight patients. Fecal fistula, the perineal type, developed in 6 patients and occurred in 4 of the 12 patients upon whom an anterior resection of the left colon was performed. Pelvic abscesses developed in four patients and a subphrenic abscess in one. Acute thrombophlebitis of the lower extremity occurred in three patients.

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37. Hinton, J. W., and Localio, S. A.: One-Stage Resection and Anastomosis of the Colon; Utilizing the Furniss Clamp, Ann. Surg. **127**:12, 1948.

RESULTS OF FOLLOW-UP AND SURVIVAL RATES

All of the 75 patients who recovered from surgery were followed. The shortest follow-up was 2 months and the longest 66 months. At present 32 (42.6%) of these patients are living. Forty-three (57.4%) have died; of this number, 42 (97.6%) died as a result of local recurrence or of metastases, and 1 died of perforation of the bowel. The highest mortality occurred in the group of patients with lesions of the splenic flexure (100%), with an average survival time of eight months. In patients with lesions in the remaining segments of the colon, the mortality and survival rates were as follows: in transverse colon lesion (71%), an average survival of 8 months; in rectosigmoid or rectal lesion (66%), an average survival of 10.5 months; in cecal and ascending colon lesion (57%), an average survival of 20.2 months; in a sigmoid lesion (50%), an average survival of 14 months. The longest survival in this group of 43 patients was 39 months, with an over-all average of 13.1 months. In those cases in which a curative resection was performed, the average survival time was 20.5 months.

It is important to note that of this group of 43 patients who died, 28 (65.3%) had a palliative resection because of local extension of the disease or distant metastases. The longest survival in this group was 39 months, with an average survival rate of 10.1 months.

In the 15 patients in whom a curative resection was done in the above groups, 3 had involvement of local lymph nodes and intravascular invasion, with an average survival rate of 18 months; in 6 patients in whom the lesion had penetrated the bowel wall, the average survival rate was 16.9 months; in 4 with involvement of local lymph nodes, intravascular invasion, and penetration of the lesion through the bowel wall, the average survival time was 16 months, and in 2 patients with the lesion limited only to the bowel, the average survival time was 17 months.

Of the 45 patients upon whom curative procedures were performed, 28 (62.2%) are living; the longest survival time is 66 months, and the shortest 7 months, the average survival rate for this group being 27.3 months. The longest survivors, to date, are those patients who had lesions of the ascending and transverse colon, rectum, and sigmoid. The greatest number of survivors were in the group with lesions involving the cecum or sigmoid; the survival rate for patients with cecal lesions is 85.7%, sigmoid 83.3%, ascending colon 66.6%, rectosigmoid 57.1%, and rectal 47%.

Of the group of patients who are alive, in two with involvement of local lymph nodes, the average survival time to date is 12.5 months; one with involvement of local lymph nodes and intravascular invasion is alive at 39 months; in eight with only local penetration of the bowel by the lesion, the average survival is 28.2 months; in three with involvement of local lymph nodes, intravascular invasion, and penetration, the survival is 19.7 months; one patient who had a metastasis involving the abdominal wall on two occasions and small bowel once is still alive after 61 months (50 months following the last operation for abdominal wall recurrence), and in 17 patients with the lesion limited to bowel, the average survival to date is 36.5 months.

Of the group of 25 patients with a lesion within a distance of 15 cm. from the anal verge, in 12 an anterior resection with a primary open end-to-end anastomosis was performed, and in 13 Miles's type of abdominoperineal resection was accom-

plished. In the former group, four patients had involvement of local lymph nodes, and in the latter group only two. At present three patients (25%) in the anterior resection group have died as a result of recurrence of their disease, as compared with four (33%) in the abdominoperineal resection group. In both groups the deaths have occurred in patients with no evidence of involvement of lymph nodes.

Anterior primary resection was performed in this group for lesions the lower limits of which ranged from 7 to 15 cm. The average survival rates at present in the two groups are as follows: in the anterior resection series, 21 months, and in the abdominoperineal series, 24.4 months. The longest survival in the two series is 39 months. Of the patients who died, the lesions in the anterior resection group were located at 7-, 8-, and 13- cm. levels, as compared with 6-, 9-, 10-, and 12- cm. levels in the abdominoperineal resection group.

The survival rates, according to Rhoads,[14] for the University of Pennsylvania group are 50% five-year survival for sigmoid lesions, 40% for transverse colon and cecum, and 37.5% for Miles's operation for lesions of the rectosigmoid and rectum. In 272 cases reported by Dixon [38] five-year survival was 67.7% with a slight increase in survival in those patients in whom the lesion was 11 to 20 cm. above the anal verge. Cattell,[39] in 79 cases of abdominoperineal resection, reported a five-year survival in 53.6%. Gilchrist and David,[40] in 153 cases of carcinoma of the rectum and rectosigmoid in which Miles's operation was performed in 140 cases, revealed a five-year survival period in 37.5% of the patients with lymph node involvement, as compared with 74.4% survival in those without involvement of lymph nodes. Hayden,[41] in 98 patients with rectal carcinoma operated on by Miles's procedure had a 33% survival rate. In 905 cases of Miles's procedure or posterior resection in cases of rectal carcinoma, Dukes's [42] studies revealed that the five-year survival rates were 47% for the former operation and 44.9% for the latter. Thomas and co-workers,[10] in 175 Miles's procedures since 1941, reported a 45.5% five-year survival. Colcock [43] studied 146 rectal carcinomas and reported a 60% five-year survival in cases with a local lesion and 30.2% in cases with lymph node metastasis. Coller and his associates,[44] in 1952 reported a 55.6% five-year survival in a group of 435 cases of cancer of the rectum and rectosigmoid in which abdominoperineal resections were performed. In 74 cases in which an anterior resection was carried out, the five-year survival rate was 66.2%. The latter operation was performed for lesions with a more favorable location.

38. Dixon, C. F.: Anterior Resection for Malignant Lesions of the Upper Part of the Rectum and Lower Part of the Sigmoid, Ann. Surg. **128**:425, 1948.

39. Cattell, R. B.: Carcinoma of Colon and Rectum: A Report of 503 Patients Treated at the Lahey Clinic 1938-1941, Inclusive, Surgery **14**:378, 1943.

40. Gilchrist, R. K., and David, V. C.: A Consideration of Pathological Factors Influencing 5 Year Survival in Radical Resection of the Large Bowel and Rectum for Carcinoma, Ann. Surg. **126**:421, 1947; Prognosis in Carcinoma of the Bowel, Surg., Gynec. & Obst. **86**:359, 1948.

41. Hayden, E. P.: The Surgical Treatment of Carcinoma of the Rectum: Statistics on 198 Cases of Resection, New England J. Med. **233**:81, 1945.

42. Dukes, C. E.: The Surgical Pathology of Rectal Cancer: President's Address, Proc. Roy. Soc. Med. **37**:131, 1944.

43. Colcock, B. P.: Prognosis in Carcinoma of Colon and Rectum: Ten Year Follow-Up of 337 Patients, Surg., Gynec. & Obst. **85**:8, 1947.

44. Coller, F. A.; Lillie, R. H.; Bryant, M. F., Jr., and Brown, W. E., III: Cancer of the Rectum: A Study of Long-Term Survival, Ann. Surg. **135**:841, 1952.

SUMMARY AND CONCLUSIONS

A complete study of the results of the surgical treatment of 80 patients with cancerous lesions of the colon is presented. A curative procedure was performed in 47 (58.7%), and a palliative operation in 32 (40%). The postoperative mortality was 2.5% in the operative group and 6.2% in the palliative group.

Over 62% of the patients in the group upon whom a curative procedure was performed are living, with an average survival rate of over 27 months. The highest survival rates were found in the group of patients with lesions of the cecum, sigmoid, ascending colon, and rectosigmoid.

Forty-three (57.4%) of 75 patients who survived surgery have died. Death in all but one was due to local and/or distant metastasis, with the highest mortality occurring in patients with lesions of the splenic flexure and transverse colon. In this group, 28 (65.3%) were patients upon whom a palliative resection was performed. The average survival rate was 10.1 months, as compared with 17 months for the curative operative group who died.

The higher the lesion is in the rectum, rectosigmoid, or sigmoid areas, the longer is the survival period and the higher are the percentages of survivals. In general, patients with lesions involving the lower left colon, have a better chance for longer survival if the lesion is in the sigmoid, being 83% for this site in this series, as compared with 57% in the rectosigmoid, and 47% in the rectum.

The results, to date, in this series of patients who had a primary anterior resection with an open end-to-end anastomosis for carcinoma of the colon within a distance of 7 to 15 cm. from the anal verge are as favorable or slightly better than in a similar group upon whom Miles's abdominoperineal resection was performed.

CARCINOMA OF THE COLON AND RECTUM

Review of Four Hundred Sixty-One Necropsy Cases at Cook County Hospital from 1929 to 1952

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IN VIEW of discrepancies in the literature concerning incidence, frequency, location, and type of metastases, as well as survival rates, in carcinoma of the colon and rectum, it appeared profitable to review the autopsy material of a large city hospital. This was done in the hope of supplementing and confirming previous findings or of unearthing relations previously not appreciated. The restriction to the use of necropsy material in a charity hospital eliminated, to a great extent, early cases. This was in part, compensated for by the size of the examined sample and by the completeness, as well as the uniformity, of the examination. In analyzing our material, the available findings in the literature were tabulated for comparison. Although this study analyzes the clinical features of autopsy cases, it also includes 128 postmortem cases in which previous definitive surgery had been done.

RESULTS

The sex incidence of carcinoma of the rectum, as compared with carcinoma of the colon, is striking. In our series of 134 cases of carcinoma of the rectum (29% of the total series reported), 70.5% of the patients were males and 29.5% were females. In the remaining 227 cases of carcinoma of the colon there was an incidence of 59.3% in males and 40.7% in females. We also found that 70% of all cases of carcinoma of the colon and rectum occurred in the white race, despite the fact that 78% of all patients admitted to the Cook County Hospital were Negroes.

In an autopsy series of this nature (Table 3) many cured lesions will be eliminated, and therefore the results of such a study will show a low incidence in the location most amenable for a cure and a higher incidence in the location less favorable for cure.[1]

From the Department of Pathology and the Hektoen Institute for Medical Research of the Cook County Hospital.

1. (*a*) Buirgie, R. E.: Carcinoma of the Large Intestine: Review of 416 Autopsy Records, Arch. Surg. **42**:801-818, 1941. (*b*) Buser, J. W.; Kirsner, J. B., and Palmer, W. L.: Carcinoma of the Large Bowel: Analysis of Clinical Features in 478 Cases, Including 88 Five-Year Plans, Cancer **3**:214-228, 1950. (*c*) Raiford, T. S.: Carcinomas of the Large Bowel: Colon, Ann. Surg. **101**:863-866, 1935. (*d*) Clogg, H. S.: Cancer of the Colon: A Study of 72 Cases, Lancet **2**:1007-1012, 1908. (*e*) Boehme, E. J., and Hanson, P. J.: Carcinoma of the Colon and Rectum: Site of Growth of 1457 Lesions, Surg. Clin. North America **26**:551-552, 1946. (*f*) Judd, E. S.: Consideration of Lesions of the Colon Treated Surgically, South. M. J. **17**:75-79, 1924. (*g*) Hayes, J. M.: The Involvement of Lymph Glands in Carcinoma of the Large Intestine, Minnesota Med. **4**:653-663, 1921. (*h*) Körte, W.: Erfahrungen über die operativen Behandlung der malignen Dickdarm-Geschwülste, Arch. klin. Chir. **61**:403-462, 1900. (*i*)

From Table 4 we can note that the metastases of tumor tissue occurred with the same relative frequency as the primary lesion, without regard to the location of the primary lesion in the colon. There is no difference in the tendency to metastasize. However, we note that lymph node metastases occurs with greater frequency in lesions of the right side of the colon than in those of the left side.

Methods of Spread of Carcinoma.—Local extension of carcinoma by infiltration constitutes one of the main methods of cancer spread. The spread also follows the course of the intramuscular lymphatics. Before the tumor has penetrated the entire wall, it may metastasize to lymph nodes. Although the carcinoma may remain localized for long periods of time once the tumor has invaded the submucosa, the lymphatics are likely to become involved. Of course, once the tumor has penetrated the entire wall it spreads more rapidly by both venous and lymphatic routes. In considering the intramural spread of carcinoma by lymphatics, one must remember that extramural metastases may occur long before the muscular coat has been penetrated by direct extension of the growth. However, this view is at variance with Dukes [2] and Grinnell,[3] who assert that lymph nodes are not involved until the bowel wall is penetrated. We do not believe that the bowel wall has to be penetrated in order for lymph nodes to be involved in the metastatic process. We have seen cases in which the bowel wall has not been completely involved, only to find far distant lymph node and visceral metastases. It is possible, however, that venous emboli may be responsible for the distant visceral metastases. It is true that venous tumor emboli may not leave any tract, and hence visceral metastases may occur without definite histologic evidence of intravenous extension. The presence of tumor cells within a vein should not be taken as prima facie evidence that distant metastases have occurred. When tumor cells are found within a vein, no certain prediction should be made that liver metastases has or has not occurred. Of the patients with visceral metastases, 71% had evidence of nodal involvement, and 3% failed to reveal involvement of lymph nodes. When the normal lymph stream is blocked by metastatic foci of tumor tissue, the direction of lymph flow is altered. The cancer cells may therefore travel in a downward, lateral, or upward direction and may be blocked at any point in the region traversed by the lymphatics with the formation of nodules. When the lym-

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Petermann, J.: Erfahrungen und Erfolge bei der operativen Behandlung des Dickdarmkrebes, ibid. **86**:53-113, 1908. (*j*) Auschutz, W.: Über den Verlauf des Ileus bei Darmcarinom und den localen Meteorismus des Caecum bei tiefsitzenden Dickdarmverschluss, ibid. **68**:195-221, 1902. (*k*) Lockhart-Mummery, J. P.: Diseases of the Rectum and Colon and Their Surgical Treatment, Ed. 2, Baltimore, William Wood and Company, 1934, pp. 352-354. (*l*) Karsner, H. T., and Clark, B., Jr.: Analysis of 104 Cases of Carcinoma of the Large Intestine, Am. J. Cancer **16**:933-970, 1932. (*m*) Allen, A. W., and Welch, C. E.: Malignant Disease of the Colon: Factors Influencing Operability, Morbidity and Mortality, Am. J. Surg. **46**:171-180, 1939. (*n*) Welch, C. E., and Giddings, W. P.: Carcinoma of the Colon and Rectum: Observations on Massachusetts General Hospital Cases 1937-1948, New England J. Med. **244**:860-867, 1951. (*o*) Dixon, C. F.; Mayo, C. W., and Remington, J. H.: Malignant Lesions of the Colon, in Practice of Surgery, Vol. 7, edited by D. D. Lewis, Hagerstown, Md., W. F. Prior Company, Inc., 1929, pp. 1-91.

2. (*a*) Dukes, C. E.: Surgical Pathology of Rectal Cancer, J. Clin. Path. **2**:95-98, 1949. (*b*) Dukes, C. E., and Bussey, H. J. R.: Venous Spread in Rectal Cancer, Proc. Roy. Soc. Med. **34**:571-573, 1941.

3. Grinnell, R. S.: The Lymphatic and Venous Spread of Carcinoma of the Rectum, Ann. Surg. **116**:200-215, 1942; Spread of Carcinoma of the Colon and Rectum, Cancer **3**:641-652, 1950.

phatics become filled with neoplastic emboli, then the lymph with tumor cells will find new unobstructed lymph channels for zones of spread. This explains retrograde metastases. Retrograde metastases of lymph nodes was found below the carcinoma

TABLE 1.—*Age and Sex Incidence of Carcinoma of the Colon and Rectum*

	Males		Females		
Age, Yr.	White	Negro	White	Negro	Total
10-19	2	0	0	0	2
20-29	3	2	4	0	9
30-39	5	4	6	9	20
40-49	25	10	22	12	69
50-59	57	11	22	8	98
60-69	77	19 (1*)	36	17	150
70-79	59	0 (2*)	23	5	89
80-89	10	0	11	1	22
Unknown	2	..	..	..	2
Total	240	46	124	48	461
	286		172		

* Members of the yellow race.

TABLE 2.—*Age Incidence of Carcinoma of the Colon and Rectum*

Decade	Allen and Welch [1m]	Buser and Co-Workers [1b]	Cook County Hospital
1st	0.0%	0.0%	0.4%
2d	0.0%	2.5%	1.9%
3d	4.6%	6.9%	4.3%
4th	18.5%	13.4%	14.9%
5th	32.0%	34.9%	21.2%
6th	29.5%	27.2%	32.5%
7th	12.6%	14.2%	19.3%
8th	1.10%	0.8%	4.7%

TABLE 3.—*Distribution of Cases, with Reference to the Primary Location of the Tumor*

	Various Authors *		Cook County Hospital	
Location of Tumor	No. of Cases	%	No. of Cases	%
Ileocecal valve	22	0.6	5	1.08
Cecum	192	5.2	46	10.00
Ascending colon	181	4.9	24	5.20
Hepatic flexure	115	3.1	19	4.12
Transverse colon	141	3.8	24	5.20
Splenic flexure	166	4.5	26	5.64
Descending colon	350	9.5	27	5.85
Sigmoid colon	684	18.5	89	19.30
Rectosigmoid colon	484	13.1	67	14.53
Rectum	1,312	35.5	134	29.05
Anorectal junction and anus	47	1.3	5	1.08
Total	3,694		461	

* Summarized average total results of 3,694 cases, as compiled by Buirgle,[1a] Buser and co-workers,[1b] Raiford,[1c] Clogg,[1d] Boehme and Hanson,[1e] Judd,[1f] Hayes,[1g] Körte,[1h] Petermann,[1i] Auschutz,[1j] Lockhart-Mummery,[1k] Karsner,[1l] Allen,[1m] Welch,[1n] and Dixon and co-workers.[1o]

of the bowel or rectum in many of our cases. For example, we have found eight carcinomas of the transverse colon (including the flexures) with lymph node metas-

TABLE 4.—*Sites of Metastases from Carcinoma of the Colon and Rectum*

	Lymph Nodes														
	Regional	Distant	Liver	Lungs *	Greater Omentum	Peritoneum	Diaphragm	Pleura	Adrenal	Ovary	Kidney	Bone †	Brain	Skin	No Metastases
Cecum	45%	43%	48%	12%	22%	22%	0.04%	0.04%	0.07%	0.07%	0.09%	.....	.....	0.06%	23%
Ascending colon ‡	29%	16%	49%	25%	0.04%	15%	0.04%	.....	0.07%	0.07%	.....	.....	0.04%	.....	29%
Hepatic flexure	47%	31%	50%	0%	1.0%	0.05%	0.05%	.....	.....	.....	0.05%	0.05%	.....	.....	37%
Transverse colon	25%	25%	30%	0.06%	12%	0.08%	.....	.....	.....	.....	.....	.....	.....	.....	50%
Splenic flexure	40%	29%	45%	11%	11%	16%	0.04%	0.08%	.....	.....	0.04%	.....	.....	.....	23%
Descending colon §	12%	6%	18%	3%	.....	4%	.....	.....	.....	.....	0.04%	.....	.....	.....	53%
Sigmoid colon	35%	23%	40%	12%	0.03%	0.05%	0.01%	0.02%	0.05%	0.05%	.....	0.04%	.....	.....	29%
Rectosigmoid	21%	21%	36%	13%	.....	6%	3%	.....	0.02%	0.02%	.....	0.02%	.....	.....	31%
Rectum	29%	16%	42%	22%	0.05%	1.8%	.....	.....	2%	.....	2%	2%	.....	.....	22%
Anorectal junction and anus	14%	....	30%	3%	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	20%

* Lungs, include hilar lymph node metastases.
† Bone, includes ribs, femur, clavicle, cervical, thoracic and lumbar vertebrae, scapula, talus, sacrum, and sternum.
‡ For the right colon (cecum to hepatic flexure) the average incidence without metastases was 29.66%.
§ For the left colon (splenic flexure to rectosigmoid) the average incidence without metastases was 34.%.

tases in the lower pelvis. It would be most probable that the upward path is the main pathway of lymphatic drainage and is the one most commonly taken by cancerous emboli.

Venous invasion seems to vary directly with the penetration of the tumor. This invasion takes place by direct continuity. However, it may also be possible that veins are invaded from neighboring lymphatic metastases. According to the work of Dukes [2a] and Grinnell [3] liver metastases were much more frequent when venous invasion was found. It is also established that there is a higher incidence of venous invasion and lymph node metastases in the annular infiltrating carcinomas. Large bulky tumors that tend to grow chiefly into the lumen of the bowel are usually slow-growing and of low-grade malignancy, whereas small deeply ulcerated tumors of higher grade malignancy tend to permeate in an outward direction into the pericolic or perirectal tissues and hence are more dangerous. These infiltrating or scirrhus tumors encircle the bowel wall and constrict the lumen to form a "napkin ring" tumor. It might be well to mention the fact that papillary tumors of the right side

TABLE 5.—*Signs and Symptoms of Colon and Rectal Carcinoma Taken as a Group*

	No. of Cases	%
Abdominal pain	318	68.9
Rectal bleeding (melena or bright-red blood)	316	68.7
Diarrhea	230	50.0
Constipation	259	56.2
Change in bowel habits (alternating constipation and diarrhea)	279	60.5
Anorexia	295	63.9
Weight loss	295	63.9
Weakness	257	55.9
Vomiting	102	22.1
Abdominal mass *	26	5.6
Jaundice	17	3.7
Distention	17	3.7

* Rectal mass, palpated in 86 cases (42%) of rectal and anal carcinoma.

of the colon offer a better prognosis (five-year survival rate) than the infiltrating neoplasm of the left side of the colon or the rectum.[4] It would seem, on the other hand, that because obstructive carcinomas of the left side of the colon (particularly rectosigmoid) are frequently diagnosed earlier the prognosis would be more favorable. A careful review of the literature seems to support the view that obstructive lesions decrease five-year survival rates, which is correlated with the added fact that these lesions have more extensive metastases. At the Cook County Hospital, lymph node involvement was present in 93% of cases of annular constricting carcinomas (including all parts of the colon and rectum), as compared with 57% in the fungating lesions. Obstruction damages the bowel wall by its penetration, and the subsequent edema makes for increased lymphatic absorption of tumor metastases. Thus the damage to the intestinal wall caused by obstruction would offer an earlier and easier road for extension.

Signs and Symptoms of Carcinoma of Colon and Rectum.—An average delay of 6.49 months occurred from the onset of symptoms to admission to the Cook County

4. Rankin, F. W., and Olson, P. F.: The Hopeful Prognosis in Cases of Carcinoma of the Colon, Surg., Gynec. & Obst. **56**:366-374, 1933.

Hospital. The duration of symptoms (without specific regard to the symptoms) were grouped in our 461 cases as follows:

Symptoms	No. of Cases	%
Less than 3 mo.	140	30.3
3-6 mo.	119	25.81
6 mo.-1 yr.	127	27.54
1-2 yr.	57	12.36
2-3 yr.	18	3.9

Of the patients, 83% had symptoms for less than one year. There were 334 patients who were not operated upon. The duration of life from the onset of their initial symptoms was 9.08 months. The duration of symptoms was somewhat longer in patients with lesions of the left side of the colon. Although obstruction due to annular scirrhus carcinomas was commoner in the rectosigmoid, the patients did not necessarily consult the physician sooner because of obstructive symptoms. The average duration of life for patients with carcinoma of the right side of the colon, from the onset of symptoms to postmortem examination, was 8.6 months, while the duration of life for patients with cancer of the left side of the colon, in the same circumstances, was 10.9 months. The average delay of 6.49 months from the onset of the disease to admission to the County Hospital was distributed as follows: The patient with the cancer of the right side of the colon entered the hospital after an average delay of 4.8 months, while the patient with the cancer of the left side entered the hospital after an average of 7.9 months. It would seem therefore that the patient with an over-all longer duration of symptoms actually entered the hospital later and consequently with more widespread disease. This correlates well with the aforementioned fact that patients with lesions of the left side had more extensive metastases. The paradoxical fact remains that the patient with more metastases lived longer, or, more possibly, that the patient lived longer for extensive metastases to develop. However, we are alert to point out that "surgical" statistics show a higher cure and survival rate when metastases are absent at the time of surgery. In 16 patients who had undergone previous surgery and in whom metastases were noted, the average duration of life following the surgery was 1.9 years.

The most important two signs and symptoms that brought the patient to the hospital were pain and rectal bleeding. The pain was almost invariably described as colicky and was associated with either complete or incomplete obstruction. In 208 cases, 46% of all cases, of carcinoma of the colon and rectum there was evidence of obstruction.

In 138 patients (30%) signs and symptoms developed referable to a complicating fistula, which included rectovesical, rectouterine, rectovaginal, and cutaneous fistulas. These symptoms ranged from hematuria in 16 cases to dysuria in 20 cases and to menorrhagia in 8 cases.

Rectal bleeding was the most prominent symptom in carcinoma of the rectum, rectosigmoid, and anus. This occurred either as melena or bright-red blood in 175 of the rectal cases (84%). In considering both the colon and the rectum this sign was present in only 68% of cases. In 78% (361) of cases chemical occult blood was present in the stools. When bleeding occurs in the right side of the colon, it becomes mixed with the liquid fecal contents of the colon so that it can be recognized only chemically. Weight loss was the most difficult sign to evaluate but varied from 10 to 100 lb. (4.5 to 45.4 kg.) in from six weeks to six months.

Change in bowel habits was present in 60.5% of our total cases. This was observed more frequently in the right half of the colon. It was seen as one of the presenting complaints. We have established the fact that constipation as a symptom occurs more frequently at the rectosigmoid, where obstruction is more likely to occur. In 65% of all cases of carcinoma of the cecum a small bowel obstruction was produced by involving the ileocecal valve. In the ampullary portion of the rectum, obstruction did not occur as frequently, but tenesmus and urinary symptoms were prominent. Complicating fistulas were noted in 30% of our cases, and 85% of all fistulas were between the ampullary portion of the rectum and the bladder, perineum, cervix, uterus, or small bowel.

The primary abdominal mass was palpated in 5.6% of all cases. The highest percentage were palpable in the cecum and in right half of the colon. Of all cecal carcinomas, 45.5% were palpable. While rectal examination revealed a positive diagnosis in an average of 47% of all rectal and anal carcinomas, the figures were not complete.

Anemia has been studied by us in only 300 cases. Of this total, 150 included the right side of the colon, 10 the transverse colon, and 140 the left side of the colon. A summary of the results is given in Table 6.

TABLE 6.—*Degree of Anemia Relative to the Primary Site of the Carcinoma*

Hemoglobin, Gm./100 Cc.	Right Colon (Cecum to Hepatic Flexure)	Midcolon	Left Colon (Splenic Flexure to Anus)
10.0 to 13.0.....	50 cases (33%)	3 cases (30%)	68 cases (48%)
8.0 to 10.0.....	45 cases (30%)	7 cases (70%)	52 cases (37%)
Less than 8.0.....	55 cases (37%)	.....	20 cases (15%)

The severer anemias were noted in lesions of the right side of the colon. In 67% of the cases with lesions of the right side and in 52% of the cases with lesions of the left side, the hemograms were of less than 10.0 gm. Owing to the fact that there were so few cases of the midcolon series, these were not included. The minimum hemoglobin content for a carcinoma of the right portion of the colon was 3.1 gm., while for a carcinoma of the left side the figure was 5.9 gm. The corresponding red blood cell counts were 1,860,000 and 3,120,000, respectively. It is certainly a well-established fact that the reason for the greater incidence of anemia in lesions of the right side of the colon is that ulceration of a large fungating mass is more likely to occur. The anemia is an iron-deficiency type.

Hemorrhoids were associated with at least 36 cases of carcinoma of the rectum and anus. In 11 of these cases, specific treatment for hemorrhoids had been given previously within a period of three years prior to later definitive surgery or post-mortem examination. A large carcinoma of the sigmoid may cause sufficient pressure on the venous return to produce associated hemorrhoids. X-ray examination was accomplished in 151 cases of the total series, and confirmed the diagnosis in 43, or 28%.

Problem of Ulcerative Colitis.—The question of complications of chronic ulcerative colitis has been investigated by us in order to determine the incidence of such complications and to analyze certain related clinical characteristics. A complete follow-up study is necessary in order to determine the actual frequency with which carcinoma appears in ulcerative colitis. In our series of 461 cases of carcinoma there were 15 cases in which a previous or associated diagnosis of chronic ulcerative colitis

had been made. We believe that the incidence of this complication may be higher than the presumptive evidence given by some authors.[5]

The commonest sites of localization in our series have been the rectum and the sigmoid. The presence of multiple separate carcinomas in cases of ulcerative colitis speaks for a definite causal relationship. In our series there were five cases, or 33%, in which multiple carcinomas could be demonstrated. The number varied from two carcinomas to diffuse carcinomatosis. A second factor that may be important in determining whether or not there is a causal effect is the age of the patient at the onset of the development of carcinoma. In our series the average age of patients at onset of the development of carcinoma was 32 years. The shortest duration of symptoms before the diagnosis was made was 4 years, but the average duration of symptoms before the diagnosis was made was 11 years [5] (Table 8). We feel therefore that the rate of incidence of carcinomatous degeneration in cases of ulcerative colitis is higher in the younger age group.

It is particularly impressive that carcinoma is revealed in so many of these cases in such an early age group, much earlier than would be expected in the general population. In two cases in our series, sidetracking operations (ileostomies and colostomy) were carried out early in the course of the disease, and this did not prevent the subsequent development of neoplasm.

TABLE 7.—*Symptoms Related to the Primary Site of the Carcinoma*

	Pain, %	Rectal Bleeding, %	Change in Bowel Habits, %	Constipation, %	Diarrhea, %	Weight Loss, %	Abdominal or Rectal Mass, %
Cecum	80.0	7.5	21.6	14.0	38.5	35.6	45.5
Ascending colon	75.5	5.7	18.6	22.8	57.7	65.5	26.7
Hepatic flexure	57.8	9.5	16.7	12.5	50.5	40.5	10.6
Transverse colon	67.5	8.6	35.5	30.6	25.1	22.6	4.1
Splenic flexure	56.7	4.7	45.6	29.6	22.1	55.8	6.8
Descending colon	46.5	5.6	65.6	37.5	33.5	65.8	5.9
Sigmoid colon	39.6	32.7	65.7	64.5	44.7	65.8	3.2
Rectosigmoid	85.7	83.5	64.7	86.9	65.6	67.8	14.5
Rectum	69.5	84.0	63.5	51.9	33.7	61.1	47.0
Anus	87.5	87.0	26.7	50.1	22.7	63.1	

Symptoms of carcinoma may actually be masked by the signs and symptoms of chronic ulcerative colitis, and the complications often overshadow the primary disease. Usually the presence of a mass arouses suspicion that a complicating malignant lesion is present. Other patients have noted a change in the character of their symptoms, which tended to indicate that a complicating malignant lesion was developing or present. This may have been an increase in the loss of weight out of proportion to the original weight loss, abdominal pain or cramps, increasing secondary anemia, increasing loss of blood in diarrheal stools, and x-ray evidence. The commonest additional factors which could be ascertained from our series were the

5. (*a*) Sloan, W. P.; Bargen, J. A., and Baggenstoss, A.: Local Complications of Chronic Ulcerative Colitis Based on the Study of 2000 Cases, Proc. Staff Meet., Mayo Clin. **25**:240-244, 1950. (*b*) Cattell, R. B., and Boehme, E. J.: Importance of Malignant Degeneration as a Complication of Chronic Ulcerative Colitis, Gastroenterology **8**:695-710, 1947. (*c*) Cattell, R. B., and Sachs, E., Jr.: Surgical Treatment of Ulcerative Colitis, J. A. M. A. **137**:929-931, 1948. (*d*) Sauer, W. G., and Bargen, J. A.: Chronic Ulcerative Colitis and Carcinoma, ibid. **141**:982-986, 1949; Chronic Ulcerative Colitis Followed by Carcinoma: Report of 26 Cases, Proc. Staff Meet., Mayo Clin. **19**:311-316, 1914.

presence of a mass and the onset of abdominal cramping pains that were the result of obstructive symptoms. The development of fistulae was occasionally encountered. In two cases metastatic lymph nodes were the initial source for making the added diagnosis. Finally, it should be mentioned that the signs and symptoms of carcinoma may be confused with an exacerbation of the ulcerative colitis.

Multiple Malignant Lesions.—In our series of 461 cases at Cook County Hospital, we have recorded 21 cases of multiple carcinomas. Of these, 7 cases, or 33%, were multiple carcinomas of the large bowel. In the remaining 14 cases the condition was associated with a carcinoma of ovary, breast, kidney, prostate, bladder, mediastinal tumor, esophagus, or stomach. From our available postmortem statistics it is extremely difficult to classify our cases as representing synchronous (occurring simultaneously) or asynchronous (occurring with an interval of time) tumors, since a great percentage of the second carcinomas were discovered as incidental autopsy findings. However, four patients who were previously operated on at the Cook

TABLE 8.—*Carcinoma as a Complication of Ulcerative Colitis*

	Sloan and Co-Workers [58a]	Cattell [58b,c]	Sauer and Bargen [58d]	Brown and Co-Workers	Cook County Hospital
No. of cases of ulcerative colitis studied	2,000	630	.....	316	.....
Pseudopolyposis	65%	.....	58.5%	40.0%	21.0%
Carcinomatous degeneration	5%	7%	.....	3.8%	.....
Average duration of symptoms prior to diagnosis	18 yr.	9 yr.	16.8 yr.	16 yr.	11 yr.
Shortest duration of symptoms before diagnosis of carcinoma was made	5 yr.	5 yr.	4 yr.	6 yr.	4 yr.
Longest duration of symptoms before diagnosis of carcinoma was made	49 yr.	.....	42 yr.	31 yr.	.....
Average age of onset of ulcerative colitis	.....	.....	.....	28.3 yr.	32 yr.
Youngest age	.....	.....	.....	13.0 yr.	.....
Oldest age	.....	.....	.....	46.0 yr.	.....
Average age of patients at onset of carcinoma	.....	.....	38.9 yr.	44.3 yr.	.....
Youngest age	.....	.....	.....	25.0 yr.	.....
Oldest age	.....	.....	.....	57.0 yr.	.....
Multiple separate carcinoma	14%	35%	.....	.....	33%

County Hospital for carcinomas of the colon returned with carcinomas of other portions of the large bowel within a period of 6 to 10 years following the initial surgery. We must also include three cases of familial polyposis in the study and five cases of multiple carcinomas associated with chronic ulcerative colitis. Immediately, the question is raised as to whether we are dealing with a metastatic lesion, recurrence, or actually a new carcinoma. Each of the tumors described by us has represented different histologic pictures, and each growth was responsible for its own group of metastases.

SUMMARY

A statistical survey of 461 necropsy cases of carcinoma of the colon and rectum at the Cook County Hospital is presented. In the total series, 29% of the lesions were carcinoma of the rectum. Of the patients the males comprised 70.5% of the total series of carcinoma of the rectum, and the females, 59.3%. The group of patients in whom carcinoma of the large bowel occurred most frequently were those between 60 and 69 years of age. In 32.5% of all cases, carcinoma occurred in this age group. However, carcinoma of the large bowel has also been seen in children as young as 14 years of age.

The liver was the most frequent site of metastases for both carcinoma of the colon and of the rectum. Metastases to the liver occurred in 39% of carcinomas of

the colon and in 36% of carcinomas of the rectum. The transverse and descending colon were the most frequent sites that revealed no metastatic lesions. The lymph nodes were involved in 28% of colonic lesions and in 20% of rectal and anal carcinomas. Far distant lymph node metastases, as well as visceral metastases, may occur without regional lymph node involvement. Once the neoplastic process has invaded the submucosa the lymphatics are likely to become involved. This explains why metastatic carcinoma in a main or intermediate lymph node near the origin of one of the main vessels may occur without involvement of regional lymph nodes near the tumor. There was good correlation between the depth of the tumor penetration and the degree of lymphatic involvement. Partial or annular constricting carcinomas comprised 46% of the total series of carcinoma of the colon and rectum, and lymph node involvement was present in 93% of these cases. Venous emboli may also explain far distant visceral metastases without local involvement. Late metastases without local recurrence occurred in 15 patients previously operated on. Local recurrence of carcinoma was highest in the rectum and rectosigmoid.

Of the patients, 83% had variable symptoms for less than one year. The duration of life from the onset of initial symptoms was nine months. The duration of symptoms is longer in patients with lesions of the left side of the colon. Although obstruction due to annular scirrhus carcinomas was commoner in the rectosigmoid, the patient did not necessarily consult the physician sooner. The most important signs and symptoms that brought the patient to the hospital were pain and rectal bleeding, which occurred in 69% of the patients. Rectal bleeding from carcinoma of the rectum occurred in 84%. Diarrhea was noted in 50% and constipation in 56%, while alternating constipation and diarrhea were noted in 61%. Vomiting occurred in 22%. An abdominal mass was noted in 45% of all patients with carcinoma of the cecum and in 27% of all patients with carcinoma of the ascending colon. A palpable rectal or anal mass was noted only in 47%. Fistulae developed in 30%. Constipation occurs more frequently at the rectosigmoid colon where obstruction is more likely to occur. In 65% of all cases, carcinoma of the cecum produced a small bowel obstruction by involvement of the ileocecal valve. Anemia of less than 8.0 gm. of hemoglobin was noted in 37% of lesions of the right side of the colon and in 15% of lesions of the left side. We have demonstrated that the course of symptoms depends upon the location of the primary tumor and upon the pathologic character of its growth. The reason for the better prognosis for lesions of the right side than for lesions of the left side of the colon can be accounted for on the basis of (1) a higher incidence of left-sided annular constricting carcinomas associated with more extensive metastases; (2) a higher rate of recurrence of carcinoma of the sigmoid and rectum, and (3) higher resectability of the lesions of the right side of the colon.

There is an increased statistical incidence of carcinoma of the colon in patients with chronic ulcerative colitis because these carcinomas appear in a younger age group and are frequently multiple. The average age of patients at onset of the development of carcinoma was 32 years. The shortest duration of symptoms before the diagnosis was made was 4 years, the average duration being 11 years. The commonest additional factor which called attention to the possibility that a malignant lesion was present was a palpable mass associated with obstruction. Multiple malignant lesions were reported in 21 cases.

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PUMP CIRCUIT FOR EXPERIMENTAL INTRACARDIAC SURGERY OF THE LEFT HEART

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SINCE the pioneering work of Gibbon [1] there has been great interest in the development of a mechanical heart-lung to allow isolation of these organs.[2] There have been numerous difficulties, and a completely satisfactory apparatus is still to be developed. Meanwhile, a number of investigators have concerned themselves with the problem of producing valvular lesions in experimental animals but have been handicapped by the lack of equipment suitable to allow direct exposure of the proper portion of the heart. Recently, several pump methods have been described for isolating the right [3] or left heart,[4] and some satisfactory valve operations have been reported.[5] The methods of shunting the blood from the left heart

From the Cardiovascular Clinic (Clinic of General Medicine and Experimental Therapeutics of the National Heart Institute, Federal Security Agency) U. S. Public Health Service Hospital.

1. Gibbon, J. H., Jr.: Artificial Maintenance of Circulation During Experimental Occlusion of the Pulmonary Artery, Arch. Surg. **34**:1105-1131 (June) 1937.

2. Miller, B. J.; Gibbon, J. H., Jr., and Gibbon, M. H.: Recent Advances in the Development of a Mechanical Heart and Lung Apparatus, Ann. Surg. **134**:694-708 (Oct.) 1951. Dennis, C.; Spreng, D. S., Jr.; Nelson, G. E.; Karlson, K. E.; Nelson, R. M.; Thomas, J. V.; Eder, W. P., and Varco, R. L.: Development of a Pump-Oxygenator to Replace the Heart and Lungs: An Apparatus Applicable to Human Patients, and Application to One Case, ibid. **134**:709-721 (Oct.) 1951. Jongbloed, J.: The Mechanical Heart-Lung System, Surg., Gynec. & Obst. **89**:684-691 (Dec.) 1949. Björk, V. O.: Brain Perfusions in Dogs with Artificially Oxygenated Blood, Acta chir. scandinav. (Supp. 137) **96**:1-122, 1948.

3. (*a*) Wesolowski, S. A., and Welch, C. S.: Experimental Maintenance of the Circulation by Mechanical Pumps, Surgery **31**:769-793 (May) 1952. (*b*) Sewell, W. H., Jr., and Glenn, W. W. L.: Experimental Cardiac Surgery: I. Observation on the Action of a Pump Designed to Shunt the Venous Blood Past the Right Heart Directly into the Pulmonary Artery, ibid. **28**:474-494 (Sept.) 1950. (*c*) Mustard, W. T., and Chute, A. L.: Experimental Intracardiac Surgery with Extracorporeal Circulation, ibid. **30**:684-688 (Oct.) 1951.

4. (*a*) Kantrowitz, A., and Kantrowitz, A.: Experimental Artificial Left Heart to Permit Surgical Exposure of Mitral Valve in Cats, Proc. Soc. Exper. Biol. & Med. **74**:193-198 (May) 1950. (*b*) Sirak, H. D.; Ellison, E. H., and Zollinger, R. M.: Cardiotomy into an Empty Left Ventricle, Surgery **28**:225-234 (Aug.) 1950. (*c*) Wesolowski.[3a]

5. (*a*) Clowes, G. H. A., Jr.: Experimental Procedures for Entry into the Left Heart to Expose the Mitral Valve, Ann. Surg. **134**:957-968 (Dec.) 1951. (*b*) Sugarman, H. J.; Wesolowski, S. A., and Welch, C. S.: Pulmonic Valve Resection Under Direct Vision, abstracted, Surgical Forum: Proceedings of the Forum Sessions, Thirty-Seventh Clinical Congress of the American College of Surgeons, San Francisco, Nov. 1951, Philadelphia, W. B. Saunders Company, 1952, p. 241. (*c*) Templeton, J. Y., III, and Gibbon, J. H., Jr.: Experimental Reconstruction of Cardiac Valves by Venous and Pericardial Grafts, Ann. Surg. **129**:161-176 (Feb.) 1949.

are cumbersome and limit the operator's access to the interior of the auricle. For this reason it is believed worth while to report a left heart pump shunt that allows ready access to any portion of the interior of the left heart. This has been developed during the past 18 months as a method for exposing the mitral valve to produce experimental stenosis.

MATERIALS AND METHODS

Healthy mongrel dogs larger than 15 kg. are anesthetized with pentobarbital sodium. Venous and arterial catheters are inserted. Positive pressure oxygen is given while the chest is open by means of a M. S. A. pneophore at pressures up to 20 cm. of water. Venous and arterial pressures are followed by suitable instruments. In some animals free plasma hemochromogen has been determined by the method of Hunter.[6] Additional studies in a few animals have included electrocardiographic recording, determination of plasma pH, measurement of venous and arterial oxygen values by the Van Slyke method, or examination of the formed blood elements.

The pump consists of a single diaphragm activated by a piston, with adjustable rate and stroke, and flap inlet and outlet valves.[7] It is described elsewhere.[8] The rate is adjustable from about 50 to 140 strokes a minute. The maximum output is 4,400 cc. a minute at a delivery pressure of 200 mm. of Hg. For dogs, however, the operation is usually at about one-half capacity. The pump parts in contact with the blood are made of polyvinyl plastic, acrylic plastic, stainless steel, or rubber. The tubes connecting the pump to the animal are composed of polyvinyl plastic. Polyethylene or acrylic cannulas are employed. A toy rubber balloon about 6 cm. in diameter has made the most serviceable input reservoir or auricle. The system is entirely closed with no air-blood interfaces and no filters. The total volume of the extracorporeal circuit, exclusive of the auricle which is rather variable, is about 100 cc. Sterilization is effected by filling the pump with aqueous benzalkonium (zephiran®) chloride 1:1,000 at least four hours prior to the experiment, and this is replaced with normal saline just before use.

Heparin sodium is given in a dose of 150 units per kilogram prior to cannulation. At the conclusion of the pumping operation 0.5 mg. per kilogram of protamine sulfate is given and repeated in 20 minutes if clotting of blood is not observed on the wound edges. Phenylephrine (neo-synephrine®) hydrochloride is administered as needed in doses of 0.1 to 0.5 mg. to support blood pressure.

The left side of the chest is opened through the fourth or fifth interspace to expose the region from the left subclavian artery to the pulmonary vein of the left lower lobe. The subclavian artery is divided and cannulated proximally with a tube 0.6 cm. in inside diameter. The right pulmonary artery is dissected out at its origin sufficiently to allow its intermittent occlusion by a glass tube and ligature without narrowing the left pulmonary artery significantly. The pulmonary vein of the left lower lobe and the adjacent auricle are dissected free, a curved clamp is placed across the auricle to give a vein stump of maximum length and, after division, the cut auricle is sewed with a continuous 00000 arterial suture. The vein is cannulated with a tube 1.2 cm. in diameter, with care not to occlude any of its tributaries. The remaining two left pulmonary veins are occluded with temporary ligatures or a serrefine clamp, and the circuit is connected as shown in Figure 1. To prevent obstruction, the reservoir outflow tube has multiple holes.

The pump is started when cannulation is complete, and a small reservoir of blood is maintained in the artificial auricle by partially occluding the outflow tube. The flow through the pump is only a fraction of the cardiac output, but it is sufficient to test the circuit and clear it of any small air bubbles. The right pulmonary artery is now occluded, shunting the entire right heart output into the left lower lobe of the lung and thence to the pump, a screw clamp on the auricle outflow tube being adjusted to keep an even reservoir volume.

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6. Hunter, F. T.; Grove-Rasmussen, M., and Soutter, L.: A Spectrophotometric Method for Quantitating Hemoglobin in Plasma or Serum, Am. J. Clin. Path. **20**:429-433 (May) 1950.

7. The pump was suggested by Dr. R. L. Bowman, Section on Technical Development, of the National Heart Institute, and was constructed by Experiment Incorporated, Richmond, Va.

8. Southworth, J. L.; Peirce, E. C., II.; Tyson, T., and Bowman, R. L.: Diaphragm Pump for Artificial Circulation, A. M. A. Arch. Surg. **66**:53-59 (Jan.) 1953.

As soon as the shunting is accomplished, the left auricle or ventricle may be opened as desired. The blood flow through the left side of the heart may be resumed at any time by simply opening the right pulmonary artery. The entire shunt is disconnected at completion of the intracardiac procedure by simply ligating the left subclavian artery and the pulmonary vein of the left lower lobe. The occlusion of the remaining veins is discontinued. The pleura and pericardium are approximated, the lung in inflated, and the chest is closed in anatomical layers as soon as protamine reversal of the heparin effect is satisfactory. Penicillin, 500,000 units, has been given postoperatively by the intramuscular route. Occasional postoperative thoracenteses have been necessary.

RESULTS

Twenty-three dogs had the blood shunted from the left heart. Their protocols are summarized in Table 1. The left side of the heart was bypassed for periods of 15 to 58 minutes and was opened for periods up to 50 minutes. Ligation of the left

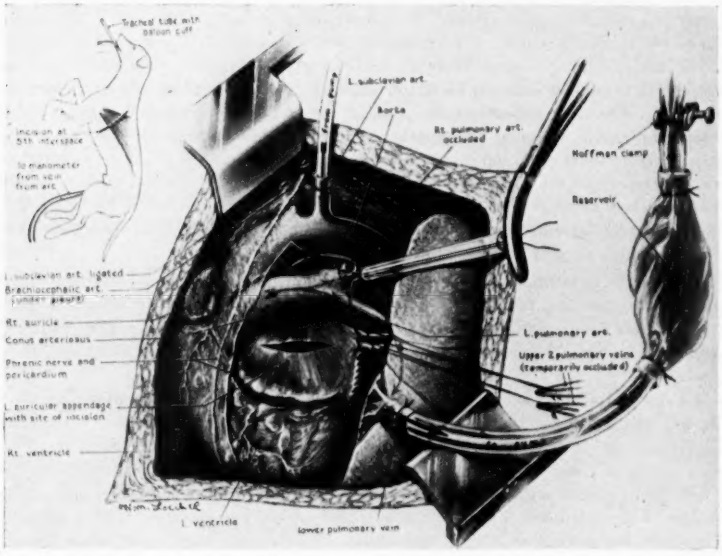

Fig. 1.—Artist's drawing showing connected pump circuit as it would be in operation and exposure of heart. Pulmonary artery blood is directed entirely to left lower lobe by occlusion of right pulmonary artery and two upper lobe pulmonary veins. Blood from left lower pulmonary vein is collected in elastic reservoir which supplies pump. Pump output is delivered into systemic circulation via left subclavian artery (brachiocephalic artery). Cannulas are arranged to occupy as little of field as possible. Lung, which must be kept inflated during the pumping, may obstruct a portion of posterior operative field.

subclavian artery has caused no difficulty, while ligation of the left lower pulmonary vein has sometimes caused marked transient postoperative congestion without necrosis of the lung. With time there has been development of visible collateral veins, and the late histological appearance of the left lower lobe is not grossly abnormal.

A total of 15 dogs survived the initial procedure and 8 of these lived to be killed or are still alive. The majority of the 15 deaths were directly attributable to technical errors associated with air emboli in six animals and hemorrhage resulting from

heparinization in four. The rigid inspection of all tubing and of the pump has decreased death from air embolism (which causes coronary artery block and ventricular fibrillation), and this accident is believed to be almost wholly preventable. Recently, all dogs have had sclerosing materials injected into the mitral valve leaflets and ring, and some deaths have been attributable to secondary ventricular fibrillation or to acute valvulitis. In addition, one dog probably died of a transfusion reaction and one of secondary hemorrhage from the subclavian artery stump.

Pressure Studies.—After an initial brief drop there is usually a relatively normal arterial pressure during shunting. Taken from the abdominal aorta, this is pulsatile and somewhat resembles a sine wave (Fig. 2). It is usually necessary to give one

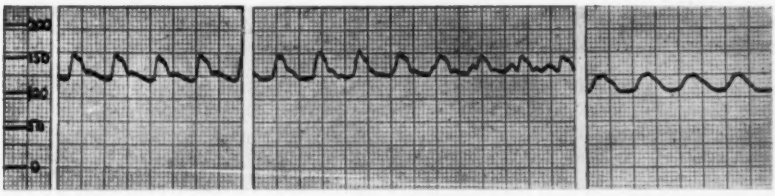

Fig. 2 (Dog 30-51).—Lower abdominal aortic pressure in millimeters of mercury recorded via femoral artery catheter, using electromanometer. Left, prior to shunting blood through pump; rate 155. Center, pump circuit on, but right pulmonary artery still open, so that some blood is going through left heart and some through pump. Right, right pulmonary artery occluded. All blood is now passing through pump circuit. Usual pulse curve has given way to one resembling sine wave; rate 150.

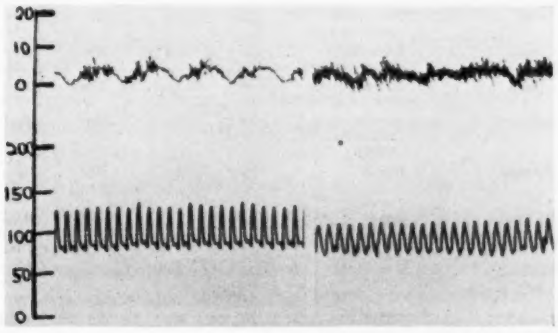

Fig. 3 (Dog 65-51).—Concomitant venous and arterial pressures in millimeters of mercury, using strain gauges and Brush recorder. Left, without pump shunt; rate 145. Right, left heart pump shunt in operation; rate 140. Venous pressure is within normal limits.

or two doses of phenylephrine during a 30-minute pumping operation to support the arterial pressure. Under the conditions of these experiments, phenylephrine generally produces both a rise in blood pressure and an increase in cardiac output, as shown by greater filling of the inflow reservoir of the pump. The venous pressure is maintained within normal limits throughout the procedure unless there is heart failure or ventricular fibrillation (Fig. 3).

Blood-Oxygen Studies.—Although blood pressure has been satisfactorily maintained and electrocardiograms have not been read as indicating myocardial ischemia,

oxygenation has not been optimal during shunting procedures. Arterial oxygen saturation was maintained between 87 and 100% in five experiments, but the arteriovenous oxygen difference was increased considerably. Venous oxygen satura-

Results of Left Heart Bypass

Dog No.	Weight, Kg.	Death	Cause	Time on Pump, Min.	Auricle Opened	Valve Procedure	Comment
67-51	20.0	During operation	Coronary air embolus	29	Yes	No	Loose pump diaphragm; technical failure
17-51	20.8	During operation	Coronary air embolus	20	No	No	From pump; technical failure
193-51	25.4	During operation	Coronary air embolus	30	Yes	No	Rupture of condom auricle; technical failure
179-51	17.5	During operation	Ventricular fibrillation	20	12 min.	Yes	Stimulation of myocardium during valve procedure
150-51	33.2	During operation	Coronary air embolus	15	13 min.	Yes	From pump; technical failure
162-51	24.1	Immediately afterward	Probable transfusion reaction	31	Yes	No	Had been a donor for a cross circulation experiment
55-52	22.0	Immediately afterward	Cardiac failure	46	37 min.	Yes	Had ventricular fibrillation following air embolus and also high-grade mitral stenosis
33-51	20.0	1 day	Shock or cardiac failure	44	No	No	Had ventricular fibrillation following air embolus; technical error
66-51	25.4	1 day	Secondary hemorrhage	30	Yes	No	Probably due to heparinization
102-51	18.9	1 day	Secondary hemorrhage	54	20 min.	Yes	Probably due in part to heparinization
71-51	33.2	1 day	Shock or anoxia	40	21 min.	Yes	Had ventricular fibrillation secondary to valve procedure; at postmortem examination had atelectasis
121-51	36.3	1 day	Secondary hemorrhage	15	No	No	Probably due to overheparinization
30-51	20.9	4 days	Secondary hemorrhage	30	No	No	Probably due in part to heparinization
152-51	16.1	4 days	Mitral valvulitis	58	50 min.	Yes	Also had pulmonary embolus or thrombosis
124-51	18.7	5 days	Hemorrhage subclavian stump	19	No	No	Technical error
56-51	28.5	3½ mo.	Killed	18	No	No	No significant abnormality left lower lobe of lung noted
62-51	17.0	6½ mo.	Killed	38	No	No	No significant abnormality left lower lobe of lung noted
128-51	17.3	9 mo.	Killed	23	Yes	Yes	Marked collateral venous circulation left lower lobe of lung
65-51	19.4	10 mo.	Killed	36	No	No	Marked collateral venous circulation left lower lobe of lung
212-51	45.0	2 wk.	Alive	57	45 min.	Yes	Held for physiologic studies
59-52	16.8	1 mo.	Alive	45	30 min.	Yes	Held for physiologic studies
38-52	22.2	6 wk.	Alive	48	32 min.	Yes	Held for physiologic studies
163-51	18.8	7 mo.	Alive	18	15 min.	Yes	Held for physiologic studies

tion ranged from 16 to 47%, compared with 61 to 83% before shunting and 52 to 59% after shunting. It is believed that this is primarily due to a drop in cardiac output secondary to interference with outflow from the left lower lobe of the lung as a result of inadequacies of the cannula, tubing, and venous reservoir. It is expected that these portions of the apparatus can be greatly improved.

Plasma pH.—Plasma pH of arterial blood during shunting has varied from 7.20 to 7.48 in four experiments. This compares with a range of 7.40 to 7.52 before and 7.27 to 7.58 after shunting. These values appear to be within a satisfactory range.

Blood Counts.—There has generally been a slight drop in the white cell count and a rise in the hematocrit level as a result of using the left pump shunt. These changes are not believed to be important.

Hemolysis.—Preoperative levels of free plasma hemochromogen have varied from 2 to 12 mg. per 100 cc. and postoperative levels from 8 to 24 mg. per 100 cc. In four instances values were determined in pumping operations of 30 to 44 minutes. These values indicate that very little hemolysis occurs.

Electrocardiograms.—Tracings taken during operation of the pump do not show changes suggestive of myocardial ischemia unless heart failure or ventricular fibrillation results from some accident. This would suggest that tissue oxygenation is satisfactory.

Blood Loss.—Because of the heparinization, there is a continuous slow loss of blood during the procedure. In addition, there is a moderate loss from the interior of the heart, requiring intermittent suction. This amounts to perhaps 3 to 15 cc. a minute. A portion of this is from the cut edge of the left auricle, but the source of the remainder has not been determined. It may be the right bronchial circulation, the intrinsic arterioluminal vessels of the ventricle, or the thebesian veins of the auricle. Incompetency of the aortic valve does not seem to play a part. An average loss during an experiment requires administration of 500 to 700 cc. of whole citrated blood.

Ventricular Fibrillation.—When this arrhythmia results from a coronary air embolus, it is usually fatal. Several dogs have been resuscitated, however, by utilizing arterial transfusion in conjunction with intermittent cardiac compression and electric shock. If it occurs as a result of endocardial stimulation, reversion may ordinarily be effected by prompt countershock. During fibrillation insufficient blood is returned to the pump, and the circulation must be supported by cardiac compression.

Use of Inflow Reservoir or Auricle.—The action of the pump is not continuous, while the pulmonary vein flow is more constant and its pulses are asynchronous with the pump. If a reservoir is not used, outflow from the lung is prevented during pump systole, and early right heart failure ensues. Better flow into the auricle is maintained if it is placed at a level below the heart, thereby exerting slight negative pressure on the pulmonary vein. This is a most critical portion of the pump circuit. Large bore tubing must be used and care taken to avoid any kinking of the vein. The use of an elastic reservoir, rather than an open one as employed by other workers, considerably simplifies the apparatus. We are now experimenting with a polyvinyl plastic reservoir of 250-cc. capacity to replace the rubber one.

Use of Bubble Trap and Filter.—It is believed that a bubble trap is unnecessary for work in experimental animals and, since it constitutes an extra piece of apparatus to watch, is undesirable where help is at a premium. An adequate bubble trap would undoubtedly have saved several dogs in this series, and no pump for use in humans should be without this protection. A filter does not appear necessary or desirable. Possible difficulties from embolic phenomena other than air occurred in only one dog.

COMMENT

A decision to utilize only one lobe of the lung to effect oxygenation of the blood was made several years ago. It seemed reasonable that the basal circulatory and oxygenation requirements of the dog could be filled easily with one-sixth to one-quarter of the pulmonary tissue. The dog, for instance, can tolerate a one-stage procedure, including left pneumonectomy and production of a large right-to-left heart shunt equivalent to 25 to 50% of the right heart output.[9] Secondary ligation of the pulmonary vein of the lower lobe did not appear to be dangerous, since the lung has a double circulation and the entire left pulmonary artery may be ligated without producing infarction of the lung.[10] Preliminary experiments in which the pulmonary vein of the left lower lobe was connected directly with the left subclavian artery indicated that the right heart could not support the systemic circulation through the pulmonary capillary bed, even under basal conditions. The experiments using the pump bear out the a priori assumptions. Blood flow and oxygenation can be satisfactory when only one lung lobe is used, and ligation of the pulmonary vein produces only temporary congestion without necrosis. After a period of months, a rather spectacular venous collateral circulation may develop. This will be further investigated.

One deficiency of the described setup is the presence of the inflated left lung in a portion of the operative field. To obviate this, attempts to use the right lung for oxygenation have been made, but this does not seem to be feasible. It is not difficult to cannulate the pulmonary vein of the right lower lobe from the left chest, but it is very difficult to isolate and occlude the remaining right pulmonary veins. It has recently been possible to return the left lower lobe to its normal position beneath the rib cage, leaving only the two upper lobes in the operative field. This has somewhat simplified the cardiac exposure.

Kantrowitz and Kantrowitz have described a method of surgical exposure of the mitral valve in cats.[4a] The two left pulmonary veins are cannulated through the auricle, making an auricular exposure rather difficult. The method otherwise appears to be satisfactory, and moving pictures of valve motions have been made.[11] A similar and somewhat improved method has been described by Clowes.[5a] This has permitted satisfactory exposure of the mitral valve for surgical manipulation. A transventricular approach to the mitral valve has been reported by Sirak, Ellison, and Zollinger, with use of an extracorporeal pump.[4b] Their method requires that blood be sucked from the left auricle itself, which must consequently be sealed from the ventricle by a tampon. This arrangement would appear not only to prevent auricular access to the mitral valve but also to introduce the problem of defoaming the collected blood. The method of Wesolowski and Welch offers similar difficulties.[3a]

9. Peirce, E. C., II: Experimental Right to Left Pulmonary Blood Shunt in Dogs, A. M. A. Arch. Surg. **63**:162-167 (Aug.) 1951.

10. Bill, A. H., Jr.: Personal communication to the authors.

11. Kantrowitz, A.; Hurwitt, E. S., and Herskovitz, A.: A Cinematographic Study of the Function of the Mitral Valve in Situ, Surgical Forum: Proceedings of the Forum Sessions, Thirty-Seventh Clinical Congress of the American College of Surgeons, San Francisco, Nov., 1951, Philadelphia, W. B. Saunders Company, 1952, pp. 204-206.

None of the left heart pump shunts are quite as effective in maintaining the circulation as a shunt utilizing another dog.[12] With the latter, ventricular fibrillation may be tolerated without cardiac compression (i. e., massage). A pump circuit is, however, somewhat simpler to set up than is a cross circulation.

It is not anticipated that this method of bypassing the left heart has direct application in humans. Relatively slight modifications of the cannulization technique, however, would permit reconstruction of the pulmonary vein of the left lower lobe, and an artery, such as the hypogastric, that could be more safely sacrificed might be used instead of the left subclavian artery. It might then be possible, with relatively simple equipment, to deal with lesions of the left heart unaccompanied by septal defects.

SUMMARY

A pump circuit that will free the entire left heart of blood is described. This permits access to the interior of the left heart for experimental surgical procedures. The entire pulmonary artery flow is directed into the left lower pulmonary lobe; the left lower pulmonary vein drains into a small elastic reservoir which supplies the pump, and the pump output is delivered to the proximal left subclavian artery. This method is very satisfactory and offers definite advantages over others reported in the literature.

The technical assistance of Alfred G. Casper, without which this project would not have been possible, is acknowledged.

12. Southworth, J. L., and Peirce, E. C., II: Cross Circulation for Intracardiac Surgery, A. M. A. Arch. Surg. **64**:58-63 (Jan.) 1952. Kerr, E.; Davis, C.; Woolsey, J., Jr.; Grimes, O.; Stephens, H. B.; Byron, R., Jr., and McCorkle, H. J.: The Maintenance of Circulation by Cross-Transfusion During Experimental Operations on the Open Heart, Surgical Forum: Proceedings of the Forum Sessions, Thirty-Seventh Clinical Congress of the American College of Surgeons, San Francisco, Nov., 1951, Philadelphia, W. B. Saunders Company, 1952, pp. 222-229.

POTASSIUM DEPLETION IN DOGS

Effect on Wound Healing, on Blood Protein and Electrolyte Levels, and on Response to Anesthesia

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THE HEALING of wounds may be influenced by the serum protein level,[1] dehydration,[2] edema, local temperature,[3] acidosis,[4] and deficiencies of certain vitamins.[5] The purpose of the present study has been to examine the effect of potassium depletion on wound healing. As the principal intracellular cation, potassium should have an important role in the fabrication of body tissue. Measurements of other plasma electrolytes have also been made.

METHODS

Mongrel dogs were weighed, given distemper injections, and later dewormed. After the animals had survived three weeks under observation, serum sodium and potassium levels were measured with the flame photometer,[6] serum carbon-dioxide-combining power was measured by

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1. Thompson, W. D.; Ravdin, I. S., and Frank, I. L.: Effect of Hyproproteinemia on Wound Disruption, Arch. Surg. **36**:500, 1938. Thompson, W. D.; Ravdin, I. S.; Rhoads, J. E., and Frank, I. L.: Use of Lyophile Plasma in Correction of Hypoproteinemia and Prevention of Wound Disruption, ibid. **36**:509, 1938.

2. Bird, C. E., and MacKay, E. M.: Healing of Wounds: Experimental Study to Show Influence of Body Hydration, Surg., Gynec. & Obst. **54**:872, 1932.

3. Large, A., and Heinbecker, P.: Effect of Cooling on Wound Healing, Ann. Surg. **120**:727, 1944.

4. Reimers, C., and Winkler, H.: Experimentelle Untersuchungen zur Wundheilung und ihre Beeinflussung durch "Azidose" (saure Kost), Deutsche Ztschr. Chir. **241**:313, 1933.

5. Zintel, H. A.: The Healing of Wounds, S. Clin. North America **26**:1404, 1946.

6. Hald, P. M.: The Flame Photometer for Measurement of Sodium and Potassium in Biological Materials, J. Biol. Chem. **167**:499, 1947.

the method of Van Slyke,[7] and serum chloride levels were measured with a modification of the Volhard method.[8] Serum protein concentration was determined by the falling drop method of Barbour and Hamilton.[9] Arterial blood was used, and the analyses were repeated at suitable intervals throughout the study. The dogs were then given the special diet shown in Table 1. The diet of the experimental animals differed from that of the controls only in that potassium chloride was added to the diet of the latter. All animals received a multivitamin supplement.[10]

This program was continued for 12 weeks, at which time the serum potassium levels indicated that a state of potassium deficiency had been achieved in the experimental animals. The dogs were then operated upon and standard 2.5-cm. wounds were produced in the skin, anterior

TABLE 1.—*Diet Used for Potassium Depletion*

Diet*	%	Salt Mixture†	%
Commercial casein	24	$CaCO_3$	22.59
Glucose (cerelose®)	62	$CaHPO_4$ $2H_2O$	14.92
Corn oil (mazola®)	8	$MgSO_4$	10.36
Salt mixture	6	NaH_2PO_4 H_2O	23.61
Vitamin supplement (vifort,® Endo Products, Inc.)		NaCl	25.69
		$FeSO_4$ $(NH_4)_2SO_4$ $6H_2O$	1.45
		$CuSO_4$ $5H_2O$	0.52
		$MnSO_4$ $4H_2O$	0.10
		$ZnCl_2$	0.20
		Na_2SiO_3 $9H_2O$	0.72
		NaI	0.003

* Muntwyler, E.; Griffin, G. E.; Samuelsen, G. S., and Griffith, L. G.: Relation of Electrolyte Composition of Plasma and Skeletal Muscle, J. Biol. Chem. **185**:525, 1950.
† Orent-Keiles, E., and McCollum, E. V.: Potassium in Animal Nutrition, J. Biol. Chem. **140**:337, 1941.

TABLE 2.—*Cumulative Data on Tensile Strength of Wounds of Control Animals and of Animals Depleted of Potassium*

Dog No.	Skin, Gm.	Fascia, Gm.	Stomach, Mm. Hg	Condition
1129	1,550	435	42	Fair
1131	1,125	Disrupted	50	Poor
1132	1,635	3,435	56	Good
1133	1,755	1,590	24	Good
1372	2,290	845	42	Good
Control, average	1,671	1,576	32.8	
1137	2,030	Disrupted	34	Good
1142	970	1,325	36	Good
1280	1,585	1,185	34	Good
1281	1,500	Disrupted	70	Fair
Experimental, average	1,517	1,255	43.5	

rectus sheath, and stomach of both groups of animals. The gastric wound was closed in two layers with plain 000 absorbable surgical (gut) suture material, the rectus sheath was closed with plain 0 gut, and the skin was closed with interrupted mattress sutures of fine nonabsorbable surgical (silk) suture material. Open drop ether was used for anesthesia in all except three

7. Peters, J. P., and Van Slyke, D. D.: Quantitative Clinical Chemistry: Vol. 2, Methods, Baltimore, Williams & Wilkins Company, 1932.

8. Harvey, S. C.: The Quantitative Determination of the Chlorides in the Urine, Arch. Int. Med. **6**:12, 1910.

9. Barbour, H. G., and Hamilton, W. F.: The Falling Drop Method for Determining Specific Gravity, J. Biol. Chem. **69**:625, 1926.

10. The multivitamin supplement was supplied by Endo Products, Inc., Richmond Hill 18, N. Y.

animals, in which intravenous injections of pentobarbital (nembutal®) were employed. The preoperative diet was continued for nine days after operation. At this time, final blood samples were drawn, and the dogs were killed by the injection of chloroform into the heart. The wounds were immediately excised by sharp dissection. The tensile strength of the skin and fascial wounds was tested with the tensiometer method of Meade,[11] and the gastric wounds were tested by the air-inflation method of Harvey and Howes.[12] Representative sections of each wound were taken for histologic study.

RESULTS

Tensile Strength of Wounds.—In Table 2 it may be seen that the tensile strength of the skin, fascial, and stomach wounds in the experimental animals did not differ materially from that of the wounds in the control animals.

Skin: The average tensile strength of the skin wounds of the control animals was 1,671 (1,125 to 2,290) gm. For the experimental animals, the average tensile strength was 1,517 (970 to 2,030) gm.

Fascia: The average tensile strength of the control fascial wounds was 1,576 (435 to 3,435) gm. However, the low value of 435 gm. (Table 2) was obtained from a partially disrupted wound, and one other control wound was completely disrupted so that a tensile strength determination was impossible. In the experimental animals, the tensile strengths of the two fascial wounds which could be measured were 1,185 and 1,325, with an average of 1,255. Two of the wounds in this group were obviously disrupted and thus were not suitable for the determinations of tensile strength. In general, infection appeared to be the major etiologic factor in the disruption of these wounds.

Stomach: The average tensile strength of the gastrotomy wounds in the control animals was 42.8 (24 to 56) mm. Hg. The average tensile strength in the experimental animals was 43.5 (34 to 70) mm. Hg. The repair of the gastrotomy wound showing a tensile strength of 70 mm. Hg had been performed with 000 chromic gut. If this value were not used in the calculation, the average tensile strength of gastric wounds in experimental animals would be 34.7 mm. Hg.

Microscopic Appearance of Wounds.—The microscopic sections of the wounds of both groups of animals were stained with hematoxylin and eosin. There were no material differences in the appearance of the wounds of the two groups of animals.

Serum Chemistry.—The serum chemistry values are presented in Table 3.

Potassium: The average initial value for serum potassium in the control animals was 3.7 mEq. per liter, as compared with a final average of 4.6 mEq. per liter. In the experimental animals, the initial average was 4.3 mEq. per liter and the final average was 3.6 mEq. per liter. Determinations of serum potassium were also made after the animals had been on their respective diets for approximately seven weeks. At this time the average serum value for the experimental dogs (potassium-free diet) was 3.8 mEq. per liter, while that of the controls was 5.1 mEq. per liter.

11. Meade, R. H.: Tensile Strength of Paralyzed Diaphragm: Preliminary Report, J. Thoracic Surg. **2**:503, 1933.

12. Harvey, S. C., and Howes, E. L.: Effect of High Protein Diet on the Velocity of Growth of Fibroblasts in the Healing Wound, Ann. Surg. **91**:641, 1930.

As has been found by others, the experimental dogs in these studies demonstrated a marked tendency to maintain a relatively normal serum potassium level in the face of prolonged dietary potassium depletion. This preservation of a relatively normal serum potassium level in the face of prolonged dietary potassium depletion is perhaps explainable. The relatively normal serum potassium levels were probably achieved at the expense of the intracellular stores of this cation. It is well known that in patients the serum potassium level may be normal in the presence of a state of marked cellular depletion of this ion. Furthermore, since the intracellular pool of potassium in man is of the general order of 3,000 mEq., as compared with only about 60 mEq. in the extracellular fluid, the release of only a modest amount

TABLE 3.—*Cumulative Data on Serum Sodium, Potassium, Chloride, Carbon-Dioxide-Combining Power (Arterial), and Protein in Control Animals and in Experimental Animals Depleted of Potassium*

	Na mEq./L.		K mEq./L.			Cl mEq./L.		CO_2 Vol. %		Serum Protein, Gm. per 100 Cc.
Dog No.	Init.	Final	Init.	7 Wk. Depletion	Final	Init.	Final	Init.	Final	
Control Killed										
1129	130.4	147.8	3.1	5.4	4.1	105.9	108.0	47.4	45.8	4.56
1131	126.1	147.8	2.8	5.0	5.1	104.3	111.8	41.9	42.8	5.11
1132	126.1	143.5	3.1	...	4.4	101.4	110.0	....	46.7	8.78
1133	152.2	143.0	4.6	5.1	4.1	106.1	110.0	43.4	43.5	5.59
1372	135.0	143.5	4.9	4.9	5.1	107.2	108.4	48.4	46.7	7.03
Average	134.0	145.1	3.7	5.1	4.6	105.0	108.6	45.3	45.1	6.21
Experimental Killed										
1137	113.9	143.5	3.6	2.8	3.8	107.7	108.9	33.9	45.4	5.32
1142	126.1	130.4	4.1	3.3	4.6	113.6	106.7	42.8	45.4	5.14
1280	165.0	143.5	...	3.1	3.6	.....	111.6	40.1	45.1	3.43
1281	135.0	139.1	4.4	4.4	2.6	109.6	110.6	44.8	48.5	3.91
Died										
1136	127.8	.....	4.6	4.0	...	107.7	.....	39.7	....	....
1140	130.0	.....	4.1	3.3	...	105.1	.....	....	....	....
1141	143.5	.....	5.1	3.3	...	102.8	.....	33.4	....	....
1143	150.0	.....	4.2	6.1	...	107.6	.....	36.2	....	....
Average	136.4	139.1	4.3	3.8	3.6	107.7	109.4	38.7	46.1	4.45

of cellular potassium into the extracellular fluid compartment would be sufficient to raise the serum level of this ion significantly.

Sodium, Chloride, and Bicarbonate: The serum levels of sodium and chloride showed no appreciable change during the course of the experiment. The serum bicarbonate level showed an average increase of almost 7 vol. per 100 cc. in the experimental animals, while there was little change in that of the controls. These findings are in line with the demonstration by Darrow and his associates[13] that states of cellular potassium depletion may be associated with an elevated serum bicarbonate level, and they afford additional, if indirect, evidence that a state of potassium depletion was produced in our experimental animals.

Serum Protein Levels.—The serum protein levels were determined at the time the dogs were killed. The control dogs had an average of 6.2 gm. per 100 ml. of

13. Darrow, D. C.; Schwartz, R.; Iannucci, J. P., and Coville, F.: Relation of Serum Bicarbonate Concentration to Muscle Composition, J. Clin. Invest. **27**:198, 1948.

serum, while the experimental animals had an average of 4.5 gm. per 100 ml. of serum. This difference probably reflected the diminished dietary intake of the experimental dogs which resulted from the pronounced anorexia which appeared after a prolonged period of the low potassium diet. However, since no obvious difference in the quality of wound healing in the two groups was demonstrated, the difference in serum protein levels does not significantly alter the validity of the results of the experiment.

Weight Changes.—In both groups the animals lost weight. The control animals lost an average of 7.5% of body weight, and the experimental animals lost an average of 10.4% of body weight. However, if only those experimental dogs which actually were killed are considered, then the average weight loss in this group was only 3.3%.

Mortality.—Five experimental dogs died within six weeks after being given the low potassium diet. One of these had an obvious cardiac defect, but the cause of death was not apparent in the other four animals. Four experimental animals died during operation or immediately thereafter, apparently from excessive anesthesia.

COMMENT

The results of this modest series of experiments indicate that the selective depletion of body potassium over a period of 12 weeks has little, if any, effect on the quality of wound healing in dogs, as determined by microscopic examination and tensile-strength measurements. These findings are in agreement with the recently published report of Findley and Howes.[14]

While the diet employed was apparently effective in producing potassium depletion in the experimental animals, its palatability was open to question in both groups. In addition, the experimental dogs consumed a progressively smaller quantity of the potassium-free diet, whereas the control animals maintained their dietary intake at a fairly constant level.

The marked intolerance of the depleted experimental animals for anesthesia was a striking observation in these studies. Four experimental animals died during operation or within 12 hours thereafter. The first two dogs had received only one-third the usual dose of intravenously administered pentobarbital when it was noted that they were already profoundly anesthetized. The injection was interrupted immediately, but, while the animals survived the operation, they never recovered consciousness. The other two experimental dogs who died received open drop ether anesthesia, and they were given only a minimal amount of this agent. Even so, one animal died on the operating table, and his death appeared to be due to over-anesthetization. The second dog survived the operation but died several hours later without ever having reacted from the anesthesia.

The cause of this poor tolerance for anesthesia observed in the experimental animals is not clear. It is possible that a deranged liver function, the result of inadequate nutrition, was an important contributing factor. Whatever the precise etiologic factors, however, these findings support clinical observations in patients, and they serve to emphasize again the fact that the depleted mammal may have a markedly diminished tolerance for opiates and anesthesia.

14. Findley, C. W., Jr., and Howes, E. L.: Potassium and Wound Healing, Surgery **28**:970, 1950.

SUMMARY AND CONCLUSIONS

Dietary potassium depletion for 12 weeks did not appear to diminish wound healing in dogs.

Dogs depleted of potassium exhibited a markedly diminished tolerance for anesthesia.

Dogs depleted of potassium showed anorexia, diminished food intake, and a consequent fall in plasma proteins.

Dogs depleted of potassium showed no changes in plasma sodium and chloride but exhibited a definite increase in bicarbonate.

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DIAGNOSTIC LUMBAR DISK PUNCTURE

Clinical Review and Analysis of Sixty-Seven Cases

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ALTHOUGH the technique and the roentgen findings in lumbar disk puncture are reported in the literature, their clinical value has been stressed only briefly, and further clinical studies of this new diagnostic method are needed. In the following article 67 cases, with 98 disks examined, are analyzed, and a clinical review is given.

TECHNIQUE

Lumbar disk puncture was introduced by Lindblom.[1] We have used the original method, with the following modification. Instead of introducing the needle under fluoroscopic control, the posterior arch of the vertebra has been localized by the bone contact obtained with the needle, which has to be introduced just below the arch. An exposure of the roentgenologist's hands to the rays and a time-consuming adaptation of the eyes are thus avoided. The modified technique is described in the following paragraph.

The patient is in a prone position, with pads under his abdomen to reduce the lordosis. A metal centimeter scale is fixed above the vertebral column, and a lateral film, with horizontal rays, is made. On the film the introduction of the needle through the skin is calculated, and the depth to the nucleus pulposus is measured. A double needle is used. After the patient is given a local anesthesia, the outer needle from the skin to the posterior wall of the spinal canal is introduced about 8 mm. from the median line. Having passed the skin, it is introduced in a slightly more cranial direction than calculated to obtain bone contact with the posterior arch of the vertebra cranial to the disk to be examined. The straight way to the disk is just below the vertebral arch. The needle is slightly withdrawn and introduced in a somewhat caudal direction. This is repeated until the bone contact disappears, and a new lateral film is made to check the position. If not correct, a new insertion through the skin is calculated (the border of the vertebral arch can easily be localized again and is considered a fixed point). Systematic correction can thus be performed. Slight corrections are made by bending the outer part of the needle in the desired direction. The inner needle has a diameter of 0.5 mm. and a length of 10 to 12 cm. It is introduced to the depth of the nucleus, as calculated in the beginning of the examination. A mixture of 2 cc. of a 35% solution of iodopyracet (diodrast®) and of 0.5 cc. of a 5% procaine hydrochloride solution is used. The amount to be injected varies between 0.5 and 2 cc. Slight pressure may be used on injection. In a normal disk there is a greater resistance than in a degenerated one. If high pressure is needed, this indicates that the needle is in an incorrect position in the fibrous annulus and has to be corrected. The presence and distribution of pain on injection is noted. Exposures are made in frontal, oblique, and lateral positions.

From the Roentgen Department (Headed by Dr. O. Sandström) and the Surgical Department (Headed by Dr. H. Wahren), Central Hospital.

1. Lindblom, K.: (*a*) Diagnostic Puncture of Intervertebral Disks in Sciatica, Acta orthop. scandinav. **17**:231-239, 1948; (*b*) Technique and Results in Myelography and Disc Puncture, Acta radiol. **34**:321-330 (Oct.-Nov.) 1950; (*c*) Discography of Dissecting Transosseous Ruptures of Intervertebral Disks in Lumbar Region, ibid. **36**:12-16 (July) 1951.

In our material, no complications have occurred. The possible risk of the method has been discussed in the literature.[2] Only once has a complication been observed, a Staphylococcus infection of the disk.[2]

ROENTGEN FINDINGS

The pathologic anatomy of the intervertebral disk has been exhaustively described in the literature, and even the injection of contrast media in autopsy specimens has been performed.[3] Recently, detailed studies were published by Lindblom and Rexed.[4] Although this has enabled us to interpret the roentgen findings, additional experience was needed in their clinical evaluation.

In the following report, our material is analyzed as to the roentgen findings on disk puncture, plain roentgenography and myelography, and as to the clinical findings. It is divided into four groups: (*a*) normal disks; (*b*) disks without or with only slight deformity of the nucleus pulposus but with a posterior or lateral rupture and a spread of the contrast; (*c*) degenerated disks with a broad cavity instead of the oval nucleus pulposus, and (*d*) degenerated disks, as in Group C, but with a posterior or lateral rupture and a spread of the contrast. On some occasions, more than one disk has been punctured; such cases have been classified as to the most pronounced changes and clinical symptoms.

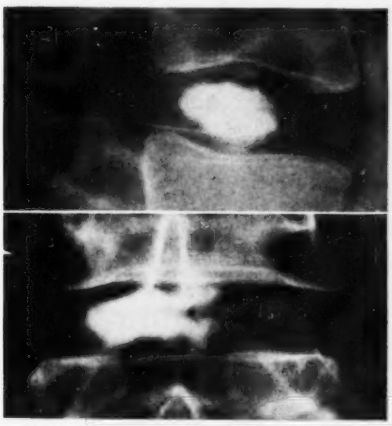

Fig. 1 (Group A).—Normal fourth-fifth lumbar disk.

A. *Normal Disks.*—This group comprises five cases, with five disks examined, of which four were between the fifth lumbar and first sacral and one was between the fourth and fifth lumbar. Puncture revealed an oval nucleus pulposus (Fig. 1).

2. Gardner, W. J.; Wise, R. E.; Hughes, C. R.; O'Connell, F. B., and Weiford, E. C.: X-Ray Visualization of the Intervertebral Disk: With a Consideration of the Morbidity of Disk Puncture, A. M. A. Arch. Surg. **64**:355-364, (March) 1952. Wise, R. E., and Weiford, E. C.: X-Ray Visualisation of the Intervertebral Disk: Report of a Case, Cleveland Clin. Quart. **18**: 127-130 (April) 1951; abstracted, Am. J. Roentgenol. **67**:679 (April) 1952.

3. Schmorl, G., and Junghanns, H.: Die gesunde und kranke Wirbelsäule im Röntgenbild und Klinik, Ed. 2, Stuttgart, Georg Thieme, 1951. Erlacher, P. R.: Nucleography, J. Bone & Joint Surg. **34B**:204-210 (May) 1952.

4. Lindblom, K., and Rexed, B.: Spinal Nerve Injury in Dorso-Lateral Protrusions of the Lumbar Disks, J. Neurosurg. **5**:413-432 (Sept.) 1948

The ordinary roentgenogram of the spine revealed a normal disk interspace, except on one occasion, when a fifth lumbar-first sacral disk had been recorded as somewhat low, apparently owing to a developmental variation. The myelogram was normal except for slight posterior bulging of the disk between the fourth and the fifth lumbar vertebrae (Table 1).

B. *Disk Rupture with Only Slight Deformity of Nucleus Pulposus.*—Of the 15 cases, with 25 disks examined, there were three fifth lumbar-first sacral disks, nine fourth-fifth lumbar disks, and three third-fourth lumbar disks. In this group the fourth-fifth lumbar disk was more frequent than in any other. The rupture usually has the appearance of a narrow channel from which the contrast is spreading to the epidural space to form a local accumulation (Fig. 2), sometimes containing particles of tissue (Fig. 3), or to spread diffusely to an extent varying from case to case. The nucleus pulposus is only slightly irregular.

The ordinary roentgenogram revealed a normal disk interspace in eight cases, in one of which there were slight spondylotic hyperostoses. There was a slight

TABLE 1.—*Myelography with Water-Soluble Contrast in Sixty-Seven Cases Examined by Disk Puncture*

Group	Roentgen Findings on Disk Puncture	No. of Cases	Myelography			
			Normal	Slight Deformities	Disk Prolapse	Not Performed
A	Normal	5	3	1	..	1
B	Rupture, but only slight deformity of nucleus pulposus	15	4	8	1	2
C	Degeneration	26	4	12	7	3
D	Rupture of degenerated disk	21	4	7	7	3

narrowing of the interspace in five, of which one had slight hyperostoses, and a narrowing to half the normal interspace in one, and even in this case hyperostoses occurred. In one, however, the interspace was even higher than ordinary and was interpreted as ballooned. The ordinary roentgenogram has thus been normal in half of all cases, and the changes, if present, have generally been slight.

Myelography (Table 1) has frequently revealed slight changes (slightly increased posterior bulging in two and irregular or thickened nerve roots in six cases). A prolapse was to be found in only one case.

For the clinical analysis, in the following heading, it is of interest that in the 10 cases with more than one disk examined there was a similar rupture in two, degeneration of the other disk in four, and a normal disk in four.

C. *Degenerated Disks.*—Of the 26 cases, with 36 disks examined, 15 of the disks were fifth lumbar-first sacral, 9 were fourth-fifth lumbar, and 2 were third-fourth lumbar. There was a broad contrast-filled space, instead of a normal nucleus, frequently extending over the whole interspace. There was no rupture and spread of the contrast (Fig. 4).

Contrary to the preceding groups, the ordinary roentgenogram has mostly been distinctly pathologic. Normal findings were recorded in only five cases, slight narrowing of the disk interspace in four, and in five others there were even small hyperostoses. Considerable narrowing and deformities were found in 10. An apparently normal interspace with small hyperostoses between the fifth lumbar and a transitional lumbosacral vertebra was noted in two cases.

Even the myelogram has been essentially pathologic (Table 1). Slight changes have been frequent; of the 12 cases, thickened nerve roots occurred in 5, slight impressions associated with root deformities in 4, and slightly increased posterior bulging of the disk in 3.

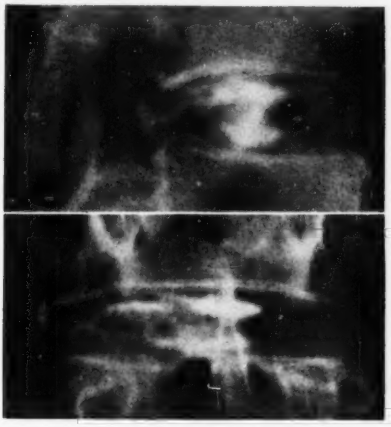

Fig. 2 (Group B).—Rupture of third-fourth lumbar disk, with posterior and lateral spread of contrast. Only slight deformity of nucleus pulposus. Radiating pain on injection (myelogram, Fig. 7*A*). No disk prolapse found on operation (Table 7, Case 7).

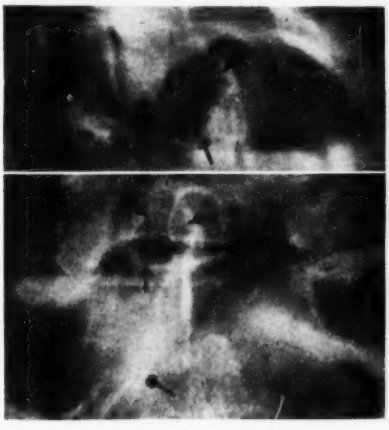

Fig. 3 (Group B).—Rupture of fifth lumbar-first sacral disk, tissue sequester (arrows) and perineural spread (blunt arrow) (myelogram, Fig. 7*B*). On operation disk prolapse found (Table 7, Case 1).

In five cases, with more than one disk examined, the other disk has been normal. In four, two disks have been punctured, with identical findings.

D. *Rupture of Degenerated Disk.*—Of the 21 cases, with 32 punctured disks, there were 9 fifth lumbar-first sacral disks, 10 fourth-fifth lumbar, and 2 third-fourth

lumbar. There was degeneration, as in Group C, but also a posterior or lateral rupture with a spreading of the contrast, which sometimes contained particles of tissue (Fig. 5).

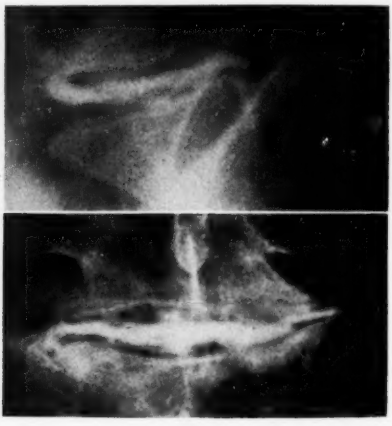

Fig. 4 (Group C).—Degenerated fifth lumbar-first sacral disk. Irregular contrast-filled space extending over the whole interspace. No spread of contrast out of disk.

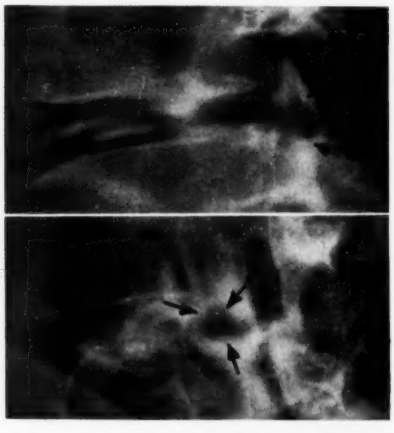

Fig. 5 (Group D).—Degeneration and rupture of fourth-fifth lumbar disk with a local epidural accumulation and diffuse spreading of contrast (the latter only to a part visible on reproduction). Tissue sequester in extruded contrast (arrows). Radiating pain on injection. Myelography and operation revealed great prolapse (Table 7, Case 5).

A normal disk interspace was found in only three, one of these between the fifth lumbar and a lumbosacral vertebra and therefore difficult to evaluate. There was a slight narrowing in two, a pronounced reduction in eight, and a reduction with hyperostoses in eight other cases. The changes were even more pronounced than in the preceding groups.

The myelogram (Table 1) has frequently revealed slight changes (slight posterior bulging or a slight impression in five cases and irregular nerve roots in two). Prolapses have occurred more frequently in this group than in any other.

Of the 11 cases with more than one disk examined, the other disk had similar changes in 4, was normal in 4, degenerated in 2, and apparently fibrosed in 1 in which there was a considerably narrowed interspace with sclerosis and with hyperostoses.

What can be learned from disk puncture for the interpretation of the ordinary roentgenogram and of the myelogram? In Group B the ordinary film revealed slight, if any, changes. On the other hand, in Groups C and D pronounced or even grave changes were to be found in most cases. The third-fourth lumbar and fourth-fifth lumbar interspace, which can be compared with both a cranial and a caudal disk, was evaluated with greater sureness than a fifth lumbar-first sacral and, especially, a fifth lumbar-transitional vertebra, which is in a transitional area, sometimes with developmental variations; slight narrowing of the latter has sometimes been overlooked, and, on the other hand, an apparently normal fifth lumbar-first sacral disk has been recorded as slightly reduced. In the myelogram, most of the slight deformities, frequently difficult to interpret, are explained by disk pathology;

TABLE 2.—*Radiating Pain on Disk Puncture in Fifty-Eight Unselected Cases**

Pain on Injection	Disk Puncture, Group			
	A	B	C	D
Present	..	7	7 (5)	8 (5)
Absent	5	6	18 (2)	7 (2)

* The number of disk prolapses included in a column is given in parentheses.

developmental variations seem to be less frequent. In general, these slight deformities are found in rupture, with spreading contrast but without tissue particles to be demonstrated on puncture; they are even frequent in the nonruptured degenerated disk. The ordinary myelographic appearance of a disk prolapse is usually found in rupture, with tissue particles in the spreading contrast or with a posterior bulging of the edges of the rupture; it may even occur in degenerated bulging disks without rupture. Two types of prolapse are thus differentiated on disk puncture, which apparently is not known in the literature. Of the lateral prolapses, invisible in the myelogram, disk puncture visualizes those of Groups B and D, with a lateral tissue particle.[5] Prolapses of Group C, if too lateral to cause any impression in the myelogram, will remain undetected even on disk puncture.

PAIN ON INJECTION

According to Lindblom,[5] sciatic pain may occur on injection of a ruptured disk and is caused by the pressure on injection. The pain may remind the patient of his usual complaints, which means that the punctured disk is the ruptured one responsible for the root or nerve compression. The injection pain may be at a higher or lower segmental level than the ordinary complaints.

My findings (Table 2) agree with the literature, since pain has been much more frequent in disks with rupture than without. It is, however, of clinical importance

5. Lindblom.[1a,b]

that radiating pain, although provoked by the pressure on injection, is not an indication for surgical treatment. This is discussed later.

Disk prolapses of Group C much more frequently cause radiating pain than those in the remaining cases of this group.

In two cases of Group C, with pain, the contrast had nearly reached the intervertebral foramen, where it had outlined a straight vertical border instead of an irregular oval, as usually found in this group. For clinical purposes, it is probably more correct to classify these as ruptures, although there is no local accumulation or spread of the contrast.

CLINICAL FINDINGS

As far as I know, no detailed analysis of the clinical findings in cases with examination by disk puncture has been published.

Pain on coughing is more frequent in disks with rupture than in those without rupture (Table 3). Numbness, however, is less frequent, especially in Group B.

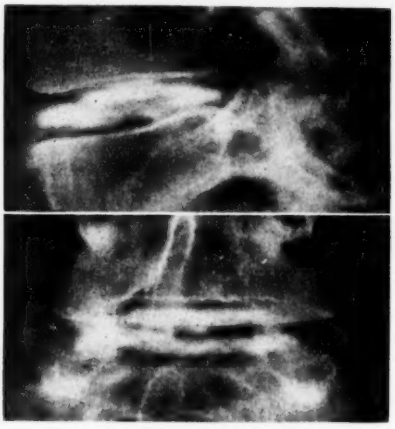

Fig. 6.—Prolapse verified at operation (Table 7, Case 3). Disk puncture does not differentiate prolapses of Group C from simple degeneration (myelogram, Fig. 7*C*).

The Lasègue sign is more frequently strongly positive (at 10 to 45 degrees) in disks with than without rupture. In simple degeneration of the disk, it occurs less frequently, although disturbances of the tendon reflexes and of the sensibility have occurred even in the latter group. In normal disks, in our material, a strongly positive and a moderate sign occur with the same frequency; apparently this group comprises sciatica of other cause than disk pathology. In some cases a negative or only slightly positive sign (at more than 80 degrees) is to be found in all groups. The Lasègue sign is dependent on the duration of the disease (Table 4). In acute cases there is much more frequently a strongly positive Lasègue sign than in long-standing cases. There are, however, differences. In Group B the Lasègue sign had mostly subsided in three months, and in cases of more than six months' duration the only sign was at more than 80 degrees. In Group C a strongly positive Lasègue sign was found in cases of various duration. Group D is the average of Groups B and C. Although the time from the first beginning of the disease is highly

variable, from a month to 20 years, the average was about the same in Groups B, C, and D, the first with only slight, if any, deformities of the disk interspace on the plain roentgenogram, the second and third with pronounced deformities in most cases.

Pain on disk injection seems to be independent of the duration of the disease. Coughing pain is more frequent in the acute cases and, in Group C, in cases with a strongly positive Lasègue sign.

TABLE 3.—*Clinical Symptoms and Signs in Fifty-Nine Unselected Cases Examined by Disk Puncture**

Clinical Symptoms and Signs	Disk Puncture, Group			
	A, 5 Cases	B, 13 Cases	C, 22 Cases	D, 19 Cases
Coughing pain	3	10 (1)	6 (2)	12 (3)
Numbness	2	.....	8 (3)	7 (3)
History of trauma	1	2 (..)	4 (2)	6 (4)
Symptoms worse after trauma	..	1 (..)	1 (1)	3 (1)
Periodicity of complaints	2	6 (..)	6 (1)	8 (..)
Average time from beginning of first symptoms, yr.	ca. 5½	8	6½	7
Average age of patient, yr.	39	41½	42	38½
Lasègue sign positive				
10-45°	2	8 (..)	10 (6)	11 (2)
46-80°	2	3 (..)	4 (..)	4 (4)
At more than 80°	1	2 (1)	7 (2)	4 (1)
Patellar reflex abnormal	..	4 (1)	3 (1)	2 (1)
Achilles reflex abnormal	2	3 (1)	10 (2)	6 (2)
Sensibility disturbance	..	2 (1)	7 (1)	5 (3)
Paresis of extensor of hallux	2	1 (..)	4 (1)	8 (3)
Rigid spine	1	3 (1)	5 (3)	8 (5)
General nervous or psychical symptoms	1	..	1 (1)	1 (..)
Spinal fluid, Nonne and Pandy tests				
Abnormal	2	6	10 (3)	1 (1)
Normal	..	2	7 (1)	11 (2)

* The number of disk prolapses included in a column is given in parentheses.

TABLE 4.—*The Lasègue Sign in Fifty-Nine Unselected Cases Examined by Disk Puncture**

Duration of Symptoms	Lasègue Sign											
	10-45°				46-80°				At More Than 80°			
	A	B	C	D	A	B	C	D	A	B	C	D
Less than 3 mo.	1	7	5 (3)	8 (1)	1	3	..	1 (1)	..	..	2	1
3-6 mo.	1	1	3 (2)	3	2	..	3	3 (3)	..	..	2	1 (1)
6-12 mo.	..	..	1	..	..	..	..	..	..	1 (1)	..	..
1-5 yr.	..	..	2 (1)	..	..	..	..	1 (1)	..	1	2 (1)	1
More than 5 yr.	..	..	..	..	..	..	..	..	..	..	2	..

* The number of disk prolapses included in each column is given in parentheses. Cases of recurrence are classified as to the latest recurrence.

A rigid spine is more frequent in disks with than without rupture; it occurs oftenest when there is rupture combined with degeneration. The Pandy and Nonne tests of the spinal fluid were positive most frequently in Group B. In Group A the positive reactions were probably caused by factors other than disk pathology. In an abnormal fourth-fifth lumbar disk, the Pandy and Nonne tests have been positive oftener than in an abnormal fifth lumbar-first sacral disk. Except for a case in Group C, there has been no pleocytosis; the highest counts, up to 6 per cubic millimeter, have been in Groups B and C.

A fourth-fifth lumbar disk has been most frequent in Group B, a fifth lumbar-first sacral disk in Group C, whereas in Group D they occurred with about equal frequency. The ruptures in Groups B and D seem to be different, mostly occurring in a relatively well-preserved fourth-fifth lumbar disk and thus without any considerable deformity of the disk interspace, but usually occurring in a degenerated fifth lumbar-first sacral disk and therefore mostly with a narrowed interspace and with hyperostoses. This is probably caused by anatomic and static differences. The

TABLE 5.—*Clinical Symptoms and Signs in Nerve Root Compression, in Irritation of the Nerve by Perineural Spread of the Nucleus Pulposus in Disk Rupture, and in Combination of the Two**

Clinical Symptoms and Signs	Compression of Nerve by Degenerated Disk Without Rupture, 22 Cases	Irritation by Perineural Spread of Nucleus Pulposus in Disk Rupture, 22 Cases	Combination of Compression and Irritation, 10 Cases
Coughing pain	6 (2)	15	5 (5)
Numbness	8 (3)	3	4 (4)
Lasègue sign			
10-45°	10 (5)	16	3 (3)
46-80°	4 (..)	3	4 (4)
At more than 80°	7 (1)	4	2 (2)
Patellar reflex abnormal	3 (1)	3	2 (2)
Achilles reflex abnormal	10 (2)	5	4 (4)
Sensibility disturbance	7 (1)	4	3 (3)
Paresis of extensor of hallux	4 (1)	5	4 (4)

* Analysis of the 54 cases with abnormal disks of Tables 3 and 4. The number of disk prolapses included in a column is given in parentheses.

TABLE 6.—*Two Syndromes Caused by the Intervertebral Disk**

Clinical Symptoms and Signs	Compression by Nonruptured Disk	Irritation by Perineural Spread of Nucleus Pulposus in Disk Rupture
Coughing pain	Found in some cases	Very frequent
Numbness	Frequent	Infrequent
Lasègue sign	Found in cases of various duration; a grave positive test is less frequent	Very frequently a grave positive sign in acute cases, mostly subsiding in 3 mo.; in cases of more than 6 mo., the sign is negative or only slightly positive
Patellar reflex abnormal	Found in some cases	Found in some cases
Achilles reflex abnormal	Frequent	Apparently less frequent
Sensibility disturbance	Frequent	Apparently less frequent
Paresis of extensor of hallux	Found in some cases	Found in some cases

* Compare with Tables 3, 4, and 5; description in text.

age of the patients cannot be the cause of the deformities, the average age of patients has even been slightly more advanced in Group B than in Group D. The patients in Group B were between 39 and 49 years of age, with only three exceptions, whereas there was a very great spread in age in Group D and, to a smaller extent, in the remaining groups.

The different findings in cases with and without rupture are of clinical importance, especially the Lasègue sign, coughing pain, and numbness. As a working hypothesis, it seems justifiable to consider the symptoms and signs to be caused by two factors, compression of the nerve and perineural infiltration by the escaped

contents of the nucleus pulposus. This parallels the two kinds of pathologic-anatomic change, degeneration of the nerve by compression and perineural fibrosis and arachnoidal proliferations around the nerve roots, as described in the literature.[4] The symptom complexes are analyzed in Tables 5 and 6; Group C is considered as pure compression and Groups B and D as irritation by the perineural spread (cases of Groups B and D, with tissue particles or with bulging edges of the rupture, evidently even causing compression, are classified as mixed forms).

FINDINGS ON OPERATION

There seems to be a confusion in the evaluation of disk puncture by the surgeon. A statement in the literature, that pain on injection is a sign of nerve root compression,[5] is misleading, since it may be interpreted as a recommendation for surgery; the fact that pain is not a reliable indicator has recently been noted by some authors.[2] Furthermore, the significance of tissue particles in the spreading contrast in rupture

TABLE 7.—*Disk Puncture in Fifteen Cases with Operations for Prolapse or for Spinal Fusion*

No. of Case	Disk	Disk Puncture, Group	Radiating Pain on Disk Puncture	Myelography	Operation
1	L5-S1	B*	Not recorded	Prolapse	Prolapse (Fig. 3)
2	L4-5	C	0	Prolapse	Prolapse
3	L5-S1 (L4-5)	C	0	Slight deformity	Prolapse (Fig. 6, 7*C*)
4	L4-5 (L3-4)	C	+	Prolapse	Prolapse
5	L4-5 (L5-Tr. v.)	D*	+	Prolapse	Prolapse (Fig. 5, 7*B*)
6	L4-5	D*	+	Prolapse	Prolapse
7	L3-4 (L4-5)	B	+	Slight deformity	Thickened nerve root (Fig. 2, 7*A*)
8	L4-5	B	+	Slight deformity	Thickened nerve root
9	L4-5	B	0	Normal	Negative
10	L5-S1	C	0	Slight deformity	Negative
11	L5-S1	C	+	Slight deformity	Negative
12	L5-S1	C	+	Prolapse	Slight general bulging of the disk; no local prolapse
13	L5-S1 (L4-5)	C	0	Not performed	Thickened ligamentum flavum
14	L5-Tr. v.	D	+	Normal	Negative
15	L4-5	D	Not recorded	Normal	Negative

* Tissue sequester.

has not been completely understood, and there are no detailed statements as to what is found on disk puncture in verified cases of prolapse.

To answer these questions, Table 7 analyzes our cases with operative findings available. What we at present are diagnosing as disk prolapse by clinical findings and by myelography and regarding as indication for surgery is not a homogeneous group if examined by disk puncture. Prolapse, verified on operation, has been found in Groups B, C, and D. The cases of Group C, without rupture, are the degenerated disks with local bulging (concealed disks). The cases of Groups B and D, with rupture, had tissue particles in the spreading contrast. In the remaining cases of Groups B and D, with negative findings on operation (except for a thickened nerve or ligamentum flavum, on some occasions), no tissue particles had been found roentgenologically. Even when there has been radiating pain on puncture, the operation did not reveal any prolapse. The epidural space is apparently

as easily emptied as it is filled with contrast on puncture, and only a lamellar space remains, which the surgeon cannot palpate. The soft contents of the nucleus pulposus, which have escaped through the rupture, are apparently not to be palpated, and the surgeon can expect to find a prolapse only in those cases in which there are tissue particles in the spreading contrast. In the pathologic anatomy, all cases with rupture and spread of the nuclear contents are classified as prolapses; theoretically, this is correct, but it is not adequate for clinical purposes. This is a new orientation. Together with the clinical findings, described in the former heading, it is a new basis for the clinical evaluation of a case and for the selection of cases for operation.

If the tissue particle in rupture is too lateral to cause an impression in the myelogram, the prolapse is diagnosed only on disk puncture.[5]

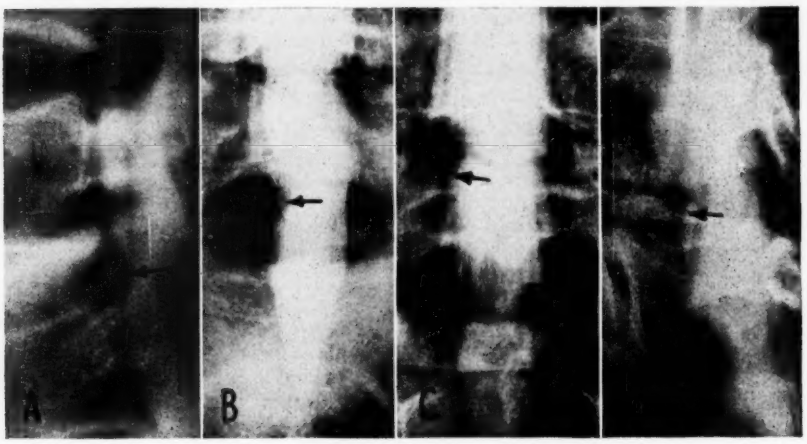

Fig. 7.—*A*, normal myelogram of third-fourth lumbar disk (upper arrow) to Figure 2. Slight bulging of fourth-fifth lumbar disk (lower arrow), on puncture with a similar rupture. *B*, myelogram to Figure 3; typical disk prolapse. *C*, deformity of nerve root between fourth and fifth lumbar (arrow) in myelogram to Figure 6.

In a degenerated disk a tissue particle may even be dislocated anteriorly.[6]

Rupture with spreading contrast, if without tissue particles, is thus no indication for surgery. The spreading nuclear contents are to be considered as a cause of clinical symptoms; the treatment, however, should be conservative. Probably some of these ruptures might be identified on operation if the disk is injected on the operation table and gives a local bulging. The surgeon, however, will find no solid tissues to extirpate. It is doubtful that incision for decompression is indicated; as seen on disk puncture, the escaping nuclear contents have a tendency to spread even without operation.

SUMMARY

A clinical analysis of 67 cases examined by disk puncture has revealed the following findings.

6. Cloward, R. B.: Anterior Herniation of a Ruptured Intervertebral Disk: Comments on the Diagnostic Value of the Diskogram, A. M. A. Arch. Surg. **64**:457-463 (April) 1952.

Pain on coughing is more frequent in disk rupture than in degenerated disks without rupture, whereas numbness is less frequent. A strongly positive Lasègue sign occurs oftener in disks with than without rupture; in simple rupture this sign usually disappears in some months, whereas in degenerated disks a strongly positive sign may be found in cases of various duration. Differences are even found in some of the other clinical symptoms and signs. As a working hypothesis, it seems justifiable to consider that two different clinical symptom complexes (syndromes) may be caused by the intervertebral disk—that of nerve root compression and that of irritation by a perineural spread of the contents of the nucleus pulposus. In many cases, there is a combination of the two.

Disk prolapse, as diagnosed by myelography and by clinical findings, is not a homogeneous group if examined by disk puncture. In most cases there is a ruptured disk. However, in rupture with spread of the contrast there is an indication for surgery only if tissue sequesters are found in the spreading contrast, or if there is a bulging of the edges of the rupture. If these conditions are absent, negative findings on operation are to be expected, even if there has been radiating pain on puncture; in these cases treatment should be conservative. In verified disk prolapse, puncture may demonstrate a degenerated disk but no rupture; those are the degenerated disks with local posterior bulging (concealed disks).

A review on lumbar disk puncture is given, and a modification of the technique, avoiding exposure of the roentgenologist's hands to the rays, is described.

SUBTOTAL ADRENALECTOMY FOR CUSHING'S SYNDROME

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ROCHESTER, MINN.

OUR EXPERIENCE at the Mayo Clinic now covers 46 cases in which subtotal adrenalectomy has been performed for Cushing's syndrome. A brief review of the activities of our medical and surgical colleagues at the Mayo Clinic in studies of abnormalities of adrenal cortex function, as related to the adrenogenital syndrome and Cushing's syndrome, seems worth while.

My interest in abnormally functioning lesions of the adrenal gland dates back to 1924, when Keyser and I [1] reported a case of carcinoma of the adrenal gland with endocrine disturbances. The patient died of adrenal cortex insufficiency after removal of the large cancerous tumor. At postmortem examination a small atrophic adrenal gland was found on the opposite side. We have since found that an atrophic gland usually exists on the side opposite a unilateral hyperfunctioning benign or malignant tumor of the adrenal cortex and that adrenal replacement therapy is essential in the preoperative and postoperative period.

In 1932 Cushing [2] described 14 patients who had signs and symptoms that simulated those associated with hyperfunctioning tumors of the adrenal cortex. The essential features were a buffalo type of obesity and hypertension, osteoporosis, ecchymosis, latent or frank diabetes, and amenorrhea or impotence. Since basophilic cells in excess or in adenomatous formation were found in the pituitary gland in these 14 cases, Cushing applied the term "pituitary basophilism" [3] to this condition.

Wilder and Kepler [4] in 1933 described four cases of pluriglandular symptoms in which the appearance was similar. Two patients who had been ill a long time seemed to have Cushing's pituitary basophilism. Of the two patients who survived only a short time, one had no tumor or histological abnormality of the pituitary gland and both had hyperplastic adrenal glands and pathological changes in the head of the pancreas. One of these two patients had a thymoma.

The next year, 1934, Wilder, Kepler and I [5] reported data on 10 patients who had the so-called suprarenal cortex syndrome. Two were found to have bilateral

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From the Division of Surgery, The Mayo Clinic.

Read at the meeting of the Chicago Surgical Society as part of a symposium on "Lesions of the Adrenal Glands and Their Treatment," Chicago, Feb. 1, 1952.

1. Keyser, L. D., and Walters, W.: Carcinoma of the Suprarenal Associated with Unusual Endocrine Manifestations, J. A. M. A. **82**:87-88 (Jan. 12) 1924.

2. Cushing, H.: Papers Relating to the Pituitary Body, Hypothalamus and Parasympathetic Nervous System, Springfield, Ill., Charles C Thomas, Publisher, 1932.

3. Cushing, H.: The Basophil Adenomas of the Pituitary Body and Their Clinical Manifestations (Pituitary Basophilism), Bull. Johns Hopkins Hosp. **50**:137-195 (March) 1932.

4. Wilder, R. M., and others: Polyglandular Dyscrasias Involving Abnormalities of Sexual Characteristics, Proc. Staff Meet., Mayo Clin. **8**:97-110 (Feb. 15) 1933.

5. Walters, W.; Wilder, R. M., and Kepler, E. J.: The Suprarenal Cortical Syndrome with Presentation of 10 Cases, Ann. Surg. **100**:670-688 (Oct.) 1934.

hyperplasia of the adrenal glands and normal pituitary glands on examination by serial section at necropsy. In two other cases bilateral exploration showed adrenal glands without gross evidence of tumors, hypertrophy, or hyperplasia. Specimens removed from each gland in both cases showed no evidence of hyperplasia on microscopic examination. A year after the operation one of the patients died at home; the pituitary gland contained an adenoma 5 mm. in diameter which was composed of basophilic cells.

Costello [6] examined 1,000 pituitary glands obtained at necropsy at the clinic in cases in which there was no history of endocrine abnormality. He found that about 200 (20%) contained adenomas, but only a fifth of the adenomas were basophilic. Similar percentages were found by Roussy and Oberling [7] in 1933. Commenting on Costello's statistics, Kepler [5] stated, "With the random incidence of basophilic adenoma, less than 4 per cent, as the foregoing seems to indicate, it must be more than a coincidence that the pathologist should have found basophilic tumors in the pituitary body in every one of ten cases in which the syndrome of 'pituitary basophilism' had been recognized." Continuing with a quotation from the same paper,[5] the following statement was made by Kepler:

> The possibility is entertained that a possible basophilic tumor of the hypophysis incites the hyperplasia and the growth of adenomas in the suprarenal glands. From the evidence at hand in this disease, however, one might speculate equally logically that the dominant part is taken by the suprarenal gland even in cases in which basophilic tumors of the hypophysis were present.

This led to Kepler's suggestion that in the absence of adrenal cortex tumors bilateral adrenal resection be done. On Sept. 5, 1932, and again on May 22, 1934, I performed such resections, removing half of each adrenal gland. The therapeutic results were not impressive. With the production by Kendall of adrenal cortex extract, which kept adrenalectomized dogs alive indefinitely, Kepler proposed in 1942 and 1943 total adrenalectomy for Cushing's syndrome. The risk of this seemed too great, and so subtotal adrenalectomy was decided on; the patients were operated on by Clagett, Priestley and me. After Kepler's death further stimulation for more radical adrenal resections was given by Sprague, whose continued study of these patients has led to outstanding contribution to their preoperative and postoperative care.

CASES STUDIED

At the meeting of the American Surgical Association in April, 1951, Priestley and I, with Sprague and Salassa,[8] presented a preliminary report of the results of subtotal adrenalectomy for Cushing's syndrome in the 29 cases in which surgical explorations did not reveal hyperfunctioning tumors. The operations were performed in the period from 1945 to January, 1951. To date, 17 additional patients have been operated on. Whereas there were six deaths among the 29 patients operated on up to January, 1951, among the 17 patients since operated on there has been only one death.

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7. Roussy, G., and Oberling, C.: Quoted in Annotation on Adenomata of the Pituitary Gland, Lancet **2**:1330 (Dec. 9) 1933.

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All the 46 patients presented a combination of clinical and laboratory findings adequate for a diagnosis of Cushing's syndrome, and most of the patients had the condition in a severe form. Many of the patients had psychotic symptoms; one had severe mental depression, and another had a mild depression, with thoughts of suicide if she should not recover. Both responded in a remarkable fashion to subtotal adrenalectomy.

Since the clinical and chemical findings in these cases have been published, suffice it to say that in the 29 cases reported last year only four of the women had normal menstrual periods. The excretion of corticosteroids in the urine was greater than normal in 23 of the 29 cases. It was normal in four and was not determined in two. About half the patients excreted a normal or less than normal amount of 17-ketosteroids, while the amount the remainder excreted was greater than normal.

Six of the 29 patients who were operated on prior to Jan. 1, 1951, died. Four of the five hospital deaths occurred in the first 10 cases, and one death occurred at home after the patient had been discharged. Of the 23 living patients, 19 have had excellent remissions from Cushing's syndrome to date. We stated in our April, 1951, paper [8] that three have had recurrences of signs and symptoms of Cushing's syndrome. One of these patients had another operation in Phoenix, Ariz., on July 27, 1951. The surgeon was a former surgical fellow at the Mayo Foundation, Dr. William H. Cleveland. The remaining portion of the adrenal gland was removed, and thus total adrenalectomy was performed. After this procedure the patient had another excellent remission of Cushing's syndrome. It is understood, of course, that replacement therapy has been carried on by administration of cortisone in this case.

We emphasized last year that it was too early to determine whether the other patients will have recurrences, and if they do what further procedures will be necessary. If the patient reoperated on by Cleveland can be used as an example, a further procedure probably should be removal of the remaining part of the gland. The results of subtotal adrenalectomy, however, have been very encouraging and have justified the continued use of this operation in 1951. We plan to continue to use it and do the operation in one stage in selected cases until definite conclusions can be reached.

A few brief comments should be made at this point regarding the results in the 17 patients (5 men and 12 women) who have undergone subtotal adrenalectomy for Cushing's syndrome since Jan. 1, 1951. However, no attempt will be made to discuss the results in this group of cases, as that will be reserved until later, when a longer time has elapsed and a detailed report can be given.

In 14 of the 17 cases [9] the preoperative values for 17-ketosteroids were within the normal range (4 to 17 mg. per 24 hours for women, 6 to 21.8 mg. for men), and in 3 cases they were low. The preoperative values for corticosteroids in urine were high in 12 cases,[10] normal in 3, and not determined in 2 cases. The normal range for corticosteroids is considered to be 0.4 to 1.2 mg. per 24 hours. In 15 of the cases excretion of 17-ketosteroids was reduced after operation (Fig. 1). In two cases values were not determined after operation. In 12 cases corticosteroids were determined both before and after operation. In 11 of these 12 the amounts were reduced after operation (Fig. 2).

9. In two of these cases there was one reading that was high and one within normal range.
10. In two cases, one preoperative reading was high and another was within normal range.

The one fatality in this series was that of a patient who made good recovery from her operation but died suddenly 27 days after operation from adrenal insufficiency at a time when an attempt was being made to determine the basic cortisone requirement. In review of the case, the outstanding point of interest seemed to be that evidence of adrenal cortex insufficiency had manifested itself by an elevation of serum potassium and a reduction of serum sodium a week or so before her death. The corollary of this certainly is that after subtotal adrenalectomy patients must be kept under constant clinical and chemical surveillance, particularly during the period

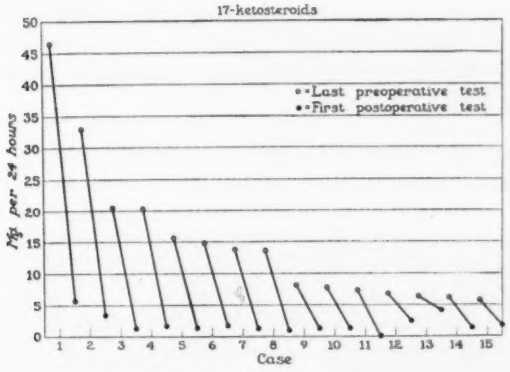

Fig. 1.—Change in values for 17-ketosteroids in urine in 15 cases in which it was determined both before and after subtotal adrenalectomy for Cushing's syndrome. The case numbers do not correspond with the cases reported in the text or in Figure 2.

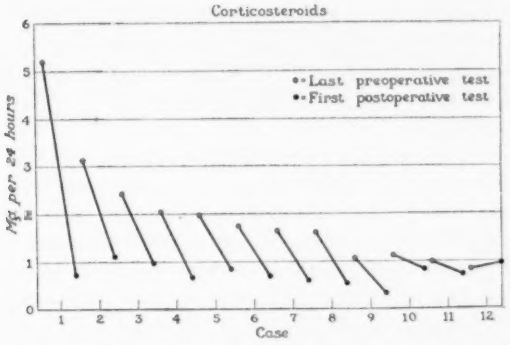

Fig. 2.—Change in values for corticosteroids in urine before and after subtotal adrenalectomy for Cushing's syndrome. Determinations were made both before and after operation in 12 cases. The case numbers do not correspond with the cases reported in the text or in Figure 1.

when basal requirements of cortisone or adrenal cortex extract or both are being determined. Most certainly, serum potassium and sodium levels should be determined as a part of the study. Also studies of reduction in the daily doses of cortisone should be done with the utmost caution and with the realization that the amount of adrenal tissue allowed to remain may degenerate from lack of vascularity soon after operation, and hence replacement therapy may have to be continued constantly.

Another point of importance is emphasized by the temporary adrenal cortex insufficiency that developed after an accident. One of our patients, aged 17 years, had had left subtotal adrenalectomy on June 14, 1951, and total right adrenalectomy on June 29, 1951. He was discharged from the clinic on July 14. Ninety-five days after his operation he was in an automobile accident. Two days after the accident and about eight hours after open reduction of a fractured clavicle adrenal cortex insufficiency developed. Before the accident the patient had been taking 25 mg. of cortisone daily. For five days he was given 50 mg. daily, but coma and hypotension occurred on the fifth day after the accident. He then was given 200 mg. daily for four days and 50 mg. on the 10th day, and then put back on his maintenance dose. He recently (Dec. 28, 1951) visited the clinic and has had an excellent remission of Cushing's syndrome, has grown in height and stature, and has a normal-appearing face, head, and body.

PREOPERATIVE PREPARATION AND POSTOPERATIVE CARE

We believe that preparation of patients with hyperfunctioning lesions of the adrenal cortex for operation by the administration of adrenal cortex extracts is an important contribution to therapy. This was first advised by Wilder, Kepler, Sprague, and their associates. At first we used extracts of the adrenal cortex prepared by Kendall for intravenous administration, and, in addition, solutions of sodium chloride and sodium lactate were given for two days prior to and following operation. Kepler also showed it was necessary at the time of operation if a hyperfunctioning tumor of the adrenal cortex was found to institute active treatment by the immediate intravenous injection of an additional quantity of adrenal cortex extracts, and that this program should be continued postoperatively over a sufficient period, usually 7 to 10 days, until the remaining adrenal gland took over the adrenal function that had been lost or greatly diminished during the hyperfunctioning activity of the adrenal cortex tumor.

As a result of these procedures and after the institution of this program there were no hospital deaths in more than 30 patients operated on at the clinic for hyperfunctioning adrenal tumors. In other words, recognition of an atrophic hyperfunctioning adrenal gland opposite the hyperfunctioning one and the use of adrenal cortex extracts as preoperative and postoperative treatment with indicated supportive measures prevented these patients from losing their lives from postoperative adrenal insufficiency. During the latter part of 1950 and in 1951, the patients operated on were given cortisone instead of the adrenal cortex extract.

What has been said referable to preoperative and postoperative treatment of the patients with hyperfunctioning adrenal cortex tumors can also be said in the management of the patients having radical subtotal adrenalectomy for Cushing's syndrome. The active treatment after operation in these cases is necessary only after the second stage of the operation in which all but 5 to 8% of the total adrenal gland substance has been removed.

In the last 25 cases cortisone has been used in the place of aqueous adrenal cortex extract in preoperative and postoperative care. The usual practice has been to give 200 mg. of cortisone acetate intramuscularly 48 and 24 hours before operation as well as the morning of the operation. In this way the immediate postoperative shock-like reaction has been averted, with one exception, without the use

of aqueous adrenal cortex extract. A delayed reaction was likely to occur from two to six weeks after operation. This was characterized by nausea, vomiting, anorexia, fever, and tachycardia. When this reaction occurred administration of cortisone for 24 to 72 hours would give relief. The intake of food then increased from virtually nothing to from 2,000 to 3,000 calories daily. When doses of cortisone were discontinued, the reaction tended to recur, but administration of cortisone would again give relief.

The effectiveness of this method of therapy when combined with the usual operative and postoperative care is evidenced by the fact that 16 of the 17 patients recovered from their operations. Positive emphasis is thus placed on its value by showing that adrenal insufficiency may cause delayed death unless adequate basic maintenance doses of adrenal cortex extracts or cortisone are given.

SUBTOTAL OR TOTAL ADRENALECTOMY

In previous years we were resecting from one-half to two-thirds of each gland, but it was not until 1945, when radical subtotal adrenalectomy was done, that it

Fig. 3 (Case 1).—Changes in patient with Cushing's syndrome after radical subtotal resection of the adrenal gland: (*a*), July 18, 1949, about one month after last stage of the operation; (*b*), Sept., 1949; (*c*), Nov. 7, 1949.

became apparent that the results depended on removal of an adequate amount of the gland tissue. In some cases remission of the syndrome was not obtained until the third operation, when the remainder of one of the resected glands was removed. This is well illustrated in the following two cases.

CASE 1.—The patient, a woman 36 years old, had had amenorrhea since 1942. In 1946, hypertension began, and fullness of the face and neck, hirsutism, facial rubor, thin dry skin, and thinning and coarsening of hair were noticeable. In January and February, 1948, bilateral sympathectomy was performed elsewhere for hypertension without benefit. Adrenal hypertrophy was noted at operation. In September, 1948, marked weakness occurred, and was followed by mental depression and loss of libido.

The patient was first seen at the Mayo Clinic in February, 1949. The blood pressure was then 200 mm. Hg systolic and 140 diastolic. She had the typical appearance described by Cushing (Fig. 3). She excreted 1.49 mg. of corticosteroids and 12 mg. of 17-ketosteroids in 24 hours. On March 12, 1949, three-fourths of the right adrenal gland was removed. The gland was normal in size and histological appearance. The patient did not improve after operation.

On May 27 three-fourths of the left adrenal gland was removed. The gland was normal in size and the cortex was hyperplastic. No clinical change resulted. Removal of the remainder, or 2 gm., of the right adrenal gland on June 24 was followed by clinical improvement. The blood pressure decreased from 200/140 to 132/98. Values for 17-ketosteroids decreased to 1.7 mg. in 24 hours and for corticosteroids to 0.33 mg. In August x-ray therapy was given to the pituitary.

One year later, in August, 1950, the patient reported by letter that she was entirely well clinically. She returned to the clinic October, 1951 (Fig. 3). A dermoid cyst was removed from the left ovary, a cyst of the right ovary was punctured, and appendectomy was performed. There was little evidence of Cushing's syndrome except elevation of blood pressure. This was 148/118 on Oct. 15 and 174/116 on Nov. 10. Studies revealed excretion of 2.3 to 2.6 mg. of 17-ketosteroids and 0.94 to 0.98 mg. of corticosteroids in 24 hours.

CASE 2.—The patient, a woman 35 years old, had begun to have hirsutism, acne, hypertension, striae, and "moon-like" facies in 1947. She was seen at the clinic in May, 1950. At that time she had the typical appearance described by Cushing, and was psychotic; the latter condition had begun while she was en route to the clinic. She excreted 18.6 mg. of 17-ketosteroids and 1.28 mg. of corticosteroids in 24 hours. On May 31, 1950, the lower half of the left adrenal gland was removed. The amount of tissue removed was 3.25 gm. and hyperplasia of the adrenal cortex with an adenoma 5 mm. in diameter was found. The right adrenal gland was explored and was found to be of normal size. From June 13 to July 25 the patient was in the Rochester State Hospital. On Aug. 8 biopsy of a rarefied area of frontal bone revealed osteoporosis and necrotic bone. On Aug. 16 progression of Cushing's symptoms was noted, and the entire right adrenal gland (7.2 gm.) was removed. The adrenal cortex was slightly hyperplastic. Since there were no changes in symptoms of Cushing's syndrome, on Oct. 6 three-fourths of the remaining part of the left adrenal gland was removed. The amount removed consisted of 2.9 gm. of infarcted hyperplastic adrenal cortex tissue. Cushing's syndrome slowly regressed (Figs. 4*a* and 5*a*). Excretion of 17-ketosteroids decreased to 1.3 mg. and corticosteroids to 0.48 mg. in 24 hours. Electroshock therapy was given on Nov. 28, and thereafter the psychosis improved (Fig. 4*b* and 5*b*).

After operation, adrenal insufficiency with weakness, hypotension, pigmentation of palms and excessive urinary excretion of chlorides were noted. These were controlled by injections of desoxycorticosterone acetate and cortisone. Two interruptions of replacement therapy resulted in symptoms of acute adrenal insufficiency. The patient was dismissed with instructions to take 12.5 mg. of cortisone twice a day by mouth and 2 mg. of desoxycorticosterone acetate sublingually daily.

At present my colleagues and I believe that about 90% of one adrenal gland should be removed and total adrenalectomy should be performed on the opposite side if satisfactory results are to be expected. With one exception, we have never performed this extensive resection of adrenal tissue in less than two operative procedures. The one exception was a recent operation in which one of us (J. T. P.) did perform the entire procedure in one stage, and the patient did well after the operation.[8] It is our plan to carry out more one-stage operations in the future in suitable cases.

The danger that the small remaining portion of the gland will atrophy must always be kept in mind, and the event was well illustrated in the case of the patient who died after subtotal adrenalectomy last year. At postmortem examination the remnant of gland that had been left behind was not viable. The possibility that the opposite adrenal gland may be destroyed by a pathological process also was brought to our attention recently.

CASE 3.—The patient was a woman with metastatic bone carcinoma following radical amputation for carcinoma of the breast, on whom a two-stage total adrenalectomy, as suggested by Huggins, was performed at the clinic. She obtained amazingly good results as regards relief of pain, which had been extremely severe, and an improvement in physical activity and the feeling of well-being. Her left adrenal gland had been almost completely replaced with carcinomatous tissue, which, of course, was unrecognized at the time of the right adrenalectomy.

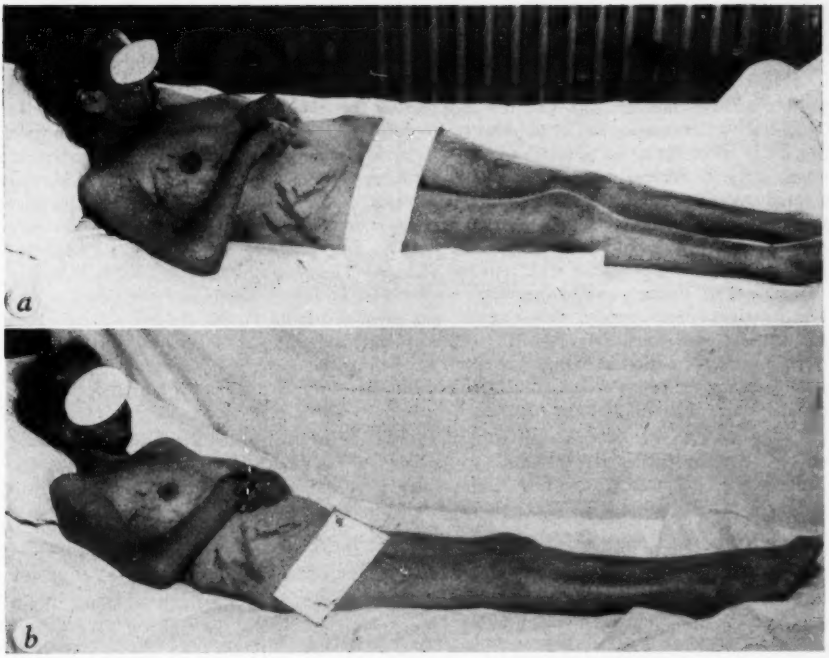

Fig. 4 (Case 2).—Patient with Cushing's syndrome: (*a*), on Nov. 20, 1950, about one month after second stage of subtotal adrenalectomy; note striae; (*b*), on Dec. 28, 1950, one month after electroshock treatment.

Fig. 5 (Case 2).—(*a*), Patient on Nov. 20, 1950, before electroshock treatment and six weeks after second stage of subtotal adrenalectomy; (*b*), Dec. 28, 1950, one month after electroshock treatment and about three months after operation.

The first operation was particularly important for this reason. It had been our intention to do a total adrenalectomy in one stage, but the patient did not do well under anesthesia and her general condition was none too good; so we thought the best procedure was to divide the operation into stages, and at the first stage removed all of the right adrenal gland. Within two hours after operation a sustained drop in blood pressure occurred, and she was treated vigorously with adrenal cortex extract and cortisone. The blood pressure returned to normal promptly. Vigorous treatment was continued for four or five days with adrenal cortex extract and cortisone on the assumption that total adrenalectomy had been done. Her postoperative progress was complicated by pneumonia with pleurisy. She recovered from this and the improvement in her general condition with relief of pain was remarkable. She wondered why it was necessary to go through another operation on the opposite side, remembering the complications after the right adrenalectomy. However, she was persuaded to do so, and the left adrenal gland was found almost completely replaced with metastatic carcinoma. Its removal was followed by little general reaction and none relating to adrenal insufficiency. She was receiving cortisone therapy during the entire period. When she returned home she was taking 25 mg. of cortisone a day and 4 mg. of buccal desoxycorticosterone (cortate®) a day, both by mouth.

On March 19th a letter was received from the patient in which she said, "I am now driving my car, attending parties and such with my friends and even did a bit of raking the other day getting our grounds ready for spring. I am so happy but almost frightened of my good fortune for fear it is too good to last. It is wonderful what was accomplished."

Among other things, this case illustrates that the loss of adrenal cortex substances by total adrenalectomy can be adequately compensated for by administration of adrenal cortex extract and cortisone, even in the presence of infection without either clinical or chemical evidence of loss of the secretion of cortex substances. However, it must be remembered that greater amounts of cortisone may be needed during infection or other intercurrent illnesses.

COMMENT

The development of surgery of the adrenal gland at the Mayo Clinic, with particular reference to subtotal adrenalectomy for the treatment of Cushing's syndrome, was sparked by Kepler's recognition of the fact that hyperfunction of the adrenal cortex produces the syndrome whether or not a basophilic adenoma of the pituitary is present and that subtotal adrenalectomy would produce a remission of the syndrome.

To the late Dr. Edwin Kepler and our medical colleagues belongs much of the rationale for the performance of subtotal adrenalectomy in these cases. To them, too, goes the credit for the metabolic studies that are so important a part of the study of the clinical hyperfunction of the adrenal cortex in Cushing's syndrome and hypofunction after removal of hyperfunctioning lesions of the adrenal cortex, both neoplastic and non-neoplastic. The use of adrenal cortex extracts and, more recently of cortisone, which were not available in 1924 when we first removed a hyperfunctioning tumor and in 1932 and 1934 when we removed half of each adrenal gland from two patients for hyperfunction has enabled us to perform radical subtotal adrenalectomy (about 95% of the glands removed) for Cushing's syndrome in 46 cases, with only seven deaths, and to operate on and remove hyperfunctioning tumors of the adrenal glands from more than 30 patients without a postoperative death from adrenal cortex insufficiency or other causes, and to do total adrenalectomy with short-term favorable results on a woman with metastatic carcinoma to bones following removal of carcinoma of the breast.

Case Reports

GASTRIC RESECTION FOLLOWED BY GANGRENE OF THE DUODENUM AND JEJUNUM WITH RECOVERY

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GANGRENE of the duodenum and afferent loop of the jejunum following subtotal gastric resection and anterior Polya anastomosis is a rare condition, and a search of the literature has revealed no report of such a case.

REPORT OF A CASE

On July 20, 1950, H. W., a 45-year-old white married woman, was admitted to the New York Hospital, complaining of persistent nausea and vomiting, with epigastric pain. Three years before admission she had first noticed knife-like epigastric pains two to four hours after meals and occasionally at 1 or 2 o'clock in the morning, which were relieved promptly by taking sodium bicarbonate or food. Up to three months before admission she had intervals of varying length when she was free from symptoms. At that time pain, nausea, and vomiting became more frequent and persistent, and during the month before entering the hospital she was in constant pain and vomited several times daily; she lost 10 lb. (4.5 kg.).

She was a thin woman, chronically ill, who obviously had lost weight. There was fullness in the epigastrium, with tenderness on palpation, but no abdominal mass could be felt. Gastric aspiration returned 1,500 cc. of watery fluid with particles of undigested food but no blood or neoplastic cells. Gastrointestinal series showed a large stomach with obstruction at the pylorus, the nature of which could not be determined, and a gastric residue of nearly 100% after eight hours. Blood, electrolytes, serum proteins, prothrombin time, and urine were within normal limits. X-rays of the chest and osseous system were normal. The electrocardiogram tracing was interpreted as showing left axis deviation but was otherwise normal.

In preparation for operation a tube was placed in the stomach, and continuous Wangensteen suction was maintained. The fluid, electrolyte, and serum protein balance was insured by daily infusions.

On July 27, 1950, with the patient under thiopental (pentothal®) sodium-cyclopropane general anesthesia, the abdomen was opened through a transverse epigastric incision. The stomach was well contracted, and on the anterior surface of the pylorus there was a large sclerosed ulcer. There were no adhesions or involvement of the pancreas or first part of the duodenum. General exploration showed no abnormality, except for a large atonic gall bladder without gross evidence of disease. With use of clamps, a subtotal gastrectomy was done without difficulty; the first portion of the duodenum was mobilized easily, and the stump was closed with three rows of interrupted fine nonabsorbable surgical (silk) sutures covered by omentum; an anterior Polya anastomosis was done without tension on or undue redundancy of the jejunum, and an incidental appendectomy was done. No blood transfusion was necessary during or after the operation. She returned to her room in good condition.

The pathologic report was benign sclerosed pyloric ulcer with sclerotic appendix.

From the Department of Surgery, New York Hospital-Cornell Medical Center.
Read before the Clinical Meeting, Cornell Medical Alumni Association, April 19, 1952.

Wangensteen suction was continued for three days, and the fluid electrolyte balance was maintained by infusions. On the afternoon of the third postoperative day, gastric suction was discontinued, and the routine progressive gastric regimen, beginning with 4 cc. of water, was started. She tolerated the routine well. She was out of bed on the first day after operation and continued to be up and about with increasing strength. The temperature curve showed no elevation above 37.8 C. after operation and reached normal four days later.

Until the ninth day after operation her course was smooth and the progressing diet was well tolerated. The temperature, pulse, and respiration were normal. During these nine days, for an unknown reason, she passed no flatus, but the abdomen was not distended, and she was not in pain. A small formed stool, with no flatus, was passed after a low enema on the sixth postoperative day. On the 10th day she was nauseated and vomited about 200 cc. of clear watery fluid, with relief. On the morning of the 11th day she complained of sharp pain in the right lower abdominal quadrant, where a tender mass 6 cm. in diameter was palpable. Twenty minutes later this mass had migrated to a point above and to the left of the umbilicus, and 30 minutes after that there was no palpable mass in the abdomen. The abdominal wall was soft and there was no tenderness, but pressure in the epigastrium produced discomfort. Aspiration of the stomach returned 850 cc. of orange-colored fluid. Wangensteen suction was started again. Scout x-rays of the abdomen showed no gas in the small or large intestine and a small gas bubble in the remnant of the stomach. There was a small crescent of gas under the left side of the diaphragm, which the roentgenologist called "residual air from the recent operation."

The temperature, pulse, respiration, and white blood cell count were normal up to the morning of the 13th postoperative day; she felt well and looked well. On the morning of the 13th day her temperature rose to 37.6 C. and pulse rate to 100, and the upper abdomen was "uncomfortable." By 3 p. m. that day her temperature was 38.1 C., pulse rate 120, and white blood cell count 15,000. Her epigastrium was full, and she had continuous dull pain. She then looked acutely ill.

She was taken to the operating room and with use of thiopental sodium-cyclopropane anesthesia the left half of the transverse epigastric scar was opened. When the peritoneal cavity was entered, there was a gush of brown odorless fluid, and a gangrenous loop of small intestine presented itself. To insure adequate exposure a left rectus incision was made downward from the transverse incision to well below the umbilicus. The gangrenous intestine proved to be the afferent loop of the gastrojejunostomy. The gangrene was sharply demarcated 2 cm. proximal to the anastomosis and extended upward to disappear under the peritoneum at the ligament of Treitz. The intestine had perforated.

The jejunum was divided just proximal to the anastomosis, without clamps. The cut edges of the divided intestine bled normally, and the opening adjacent to the gastrojejunostomy was closed with a fine silk purse-string suture reinforced with interrupted 00 chromic absorbable surgical (gut) sutures. The mesentery of the gangrenous loop of jejunum was divided to the ligament of Treitz, and the intestine was removed. The vessels of the mesentery showed no evidence of thrombosis. The duodenal stump was well healed, and the anterior surface of the duodenum looked normal. After the peritoneum was incised lateral to the duodenum, the duodenum was rolled medially, and its posterior wall was found to be gangrenous. The common bile duct was divided between clamps at the head of the pancreas and its proximal end doubly ligated with transfixion ligatures of 0 chromic gut. The duodenum was dissected from the head of the pancreas, dividing the ligating vessels as encountered. All the vessels bled, and no thrombosis was discovered. The pancreatic duct was ligated with 0 chromic gut, and the open area of the head of the pancreas was closed with closely placed mattress sutures of 0 chromic gut. The duodenum was completely removed.

Because of the extensive involvement of the peritoneal cavity and the desperate condition of the patient, it was considered unwise to implant the pancreatic duct into a loop of jejunum as a part of a Roux-Y cholecystenterostomy. A loop of jejunum 18 in. (45 cm.) from the gastrojejunostomy was secured, and, without clamps, a cholecystenterostomy was performed. A cigarette drain was passed to the bed of the third part of the duodenum under the ligament of

Treitz and a similar drain placed in the Morrison pouch and the wound closed in layers about the drains with interrupted 0 chromic gut and fine silk sutures for the skin. During the operation 1,500 cc. whole blood and 1,000 cc. of 5% glucose in distilled water were given intravenously.

On preparing to remove the patient from the operating table, it was noticed that the entire left side of her body was deeply cyanotic, while the right side was of normal color. There were no abnormal muscular reactions, and her pupils were equal and regular. Cardiac activity, blood pressure, and respirations were normal for the stage of anesthesia. With the administration of 90% oxygen the cyanosis gradually cleared, never to return. Thirty minutes later she left the operating room without cyanosis and in fairly good condition.

The pathologic report, gangrene of the small intestine, gave no suggestion of any underlying condition. Culture of the peritoneal fluid yielded nonhemolytic Streptococcus zymogenes, Escherichia coli, and Aerobacter aerogenes.

The patient was placed in an oxygen tent, and the administration of maximum effective doses of penicillin, dihydrostreptomycin, and aureomycin was started. Fluids, electrolytes, and vitamins were supplied by infusion. To maintain the serum protein level, 500 cc. of amino acids were given daily, supplemented by 1 unit of plasma. Potassium chloride was added, as indicated, to the infusions to keep the potassium level above the critical point.

By the third day after resection of the duodenum and jejunum, she was sleeping well and felt comfortable, and there was scanty drainage by Wangensteen suction. On the fourth day small amounts of water by mouth were well tolerated, and on the next day meritene® (a protein supplement) in skimmed milk, 30 cc. every 30 minutes, was added to the diet. On the sixth postoperative day a progressive six-feeding gastric diet (low fat), with 0.5 gm. pancreatin with each feeding, was started.

A pancreatic fistula was evident on the fifth day after operation, and 400 to 600 cc. of juice (enzymes demonstrated) was discharged daily for four days. The discharge from this fistula decreased rapidly, and for irregular periods there was no discharge.

Spontaneous stools were passed beginning on the sixth postoperative day, and from then until her discharge she passed from one to six soft formed stools daily.

Beginning with the fourth day after excision of the gangrenous intestine, gradual ambulation was started. She gained strength slowly and tolerated her diet well.

Forty days after the gastric resection and 27 days after the duodenojejunal resection, she left for home. At that time the pancreatic fistula was discharging an estimated 20 to 40 cc. daily. The pancreatic fistula closed spontaneously 65 days after its appearance.

Her progress was slow but steady; strength returned gradually, and there was steady, though slow, increase in weight. In October, 1951, in an attempt to aid fat digestion, 8 cc. of sorethytan (20) monooleate ("monitan") was added to each meal. This seems to have been beneficial, and, with it and the pancreatin, she tolerates small amounts of fat in her food.

On Dec. 7, 1951, she was readmitted to New York Hospital, with a history of recurring generalized abdominal cramps with nausea, vomiting, and increasing abdominal distention with no passage of flatus or stool. Operation revealed obstruction of the midjejunum by a broad firm peritoneal adhesion. This band was divided and the obstruction was relieved. The intestine was viable. Examination of the upper abdomen showed the well-placed gastrojejunostomy, a slightly thickened pancreas, and a functioning cholecystenterostomy. The liver was smooth and, aside from accentuated fibrous markings, appeared normal. The gall-bladder wall was thickened and grayish-white. There were no adhesions about the gall bladder and the jejunal loop of the anastomosis. Before discharge from the hospital 11 days after operation a gastrointestinal series showed a well-functioning gastrojejunostomy (Polya) with a cholecystenterostomy. A small amount of barium entered the gall bladder during the examination, but this was rapidly evacuated. She left the hospital in good condition with her wound well healed.

When last seen on Dec. 15, 1952, she looked well and felt strong. Since Sept. 5, 1950, she has gained 20 lb. (9.1 kg.). The abdominal wall is somewhat weak, but a light girdle supplies what little support is needed. A liberal low-fat diet, three meals supplemented with small midmorning and midafternoon snacks, is well tolerated. She tolerates small amounts of butter and some milk. The blood picture is normal, and there are no clinical evidences of nutritional deficiencies. Six to 14 somewhat bulky stools are not troublesome if she continues to use pancreatin and sorethytan (20) monooleate with her meals.

COMMENT

Any attempt to explain this fantastic and unusual case would be speculation. The gangrene of the duodenum and the first loop of the jejunum must have been vascular in origin, and the absence of involvement of the middle colic artery and of the inferior pancreaticoduodenal artery suggests anomalous blood supply.

SUMMARY

This case is reported to record an unusual complication following gastric resection with anterior Polya gastrojejunostomy.

RESECTION OF LEFT LOBE OF LIVER FOR ECHINOCOCCUS CYST

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CLEVELAND
FRED ROEMER, M.D.
BEDFORD, OHIO
AND
LEWIS O. TELLE, M.D.
CLEVELAND

THIS CASE is reported to describe a surgical maneuver designed to control hemorrhage during the operation of total or partial left hepatic lobectomy.

REPORT OF CASE

The patient was a 53-year-old white woman who was born in rural southern Italy, migrating to the Cleveland area when 8 years old. Her health was unimpaired until approximately 10 years prior to admission, when she noted progressive mild postprandial dyspepsia. In 1948 she became aware of a vague, slightly tender, continuous left epigastric fullness. One year later she began to experience episodes of deep-seated aching subxiphoid pain radiating posteriorly in a transverse and perpendicular fashion to the interscapular area. X-ray studies showed slight irregular elevation of the medial aspect of the left leaf of the diaphragm and extrinsic pressure along the prepyloric portion of the stomach. Extensive laboratory studies did not indicate evidence of hepatic, gastrointestinal, pancreatic, or biliary dysfunction. An indistinct slightly tender fullness was palpable in the left subxiphoid area. A bruit was not heard. Exploratory laparotomy revealed a 15 by 20 cm. fluctuant, grayish-white, slightly lobulated, irregularly thin- and thick-walled cystic structure within the substance of the left lobe of the liver, which protruded in an anteroinferior direction. There was no other evidence of intra-abdominal pathologic change. An aspiration biopsy was performed, removing 20 cc. of watery clear fluid containing minute white particles. The needle puncture wound was closed by suturing a piece of gelfoam® over the hole in the liver substance.

The histologic report showed that large numbers of scolices were present, characteristic of echinococcus cyst.

The mild symptoms continued for one and one-half years, until two days prior to admission, at which time she was brought to the hospital by emergency ambulance with severe lancinating pains in the usual area, associated with nausea, vomiting, and moderate shock, but without chills, fever, or jaundice. She appeared well nourished, somewhat pale, and obviously having severe upper midabdominal pain. The attacks subsided and reappeared at intervals of a few hours for several days.

General physical examination did not reveal any abnormalities other than those previously encountered in the midupper abdomen. There was moderate tenderness over the mass, which moved with respiration. Laboratory and roentgen studies were as before.

The patient consented to operation when she saw that the attacks were becoming severer. After suitable preparation, laparotomy was performed through a high right rectus incision, with use of tetracaine (pontocaine®) hydrochloride spinal anesthesia. The left lobe of the liver was obscured by many firm adhesions between it, the diaphragm, the falciform ligament, the stomach, and the greater omentum. These were carefully separated, revealing a greatly enlarged lobe almost completely replaced by a mass measuring 15 by 20 by 15 cm. with gross characteristics similar to those previously encountered.

Chief of Surgery, Dr. Renner, and Resident in Surgery, Dr. Telle, Doctors Hospital.

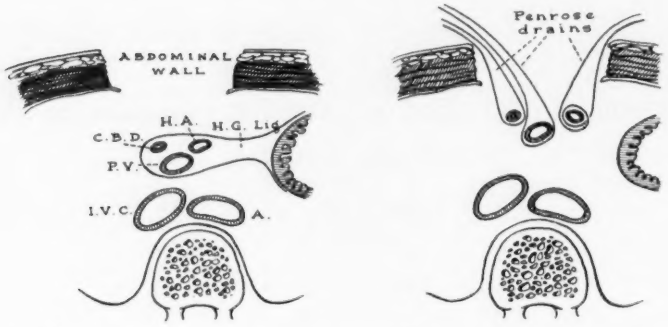

Fig. 1.—Cross sectional diagrams showing structures in the hepatoduodenal ligament before and after dissection and elevation with small-sized Penrose drains: *C. B. D.*, common bile dust; *H. A.*, hepatic artery; *P. V.*, portal vein; *H. G. Lig.*, hepatoduodenal ligament; *I. V. C.*, inferior vena cava, and *A.*, aorta.

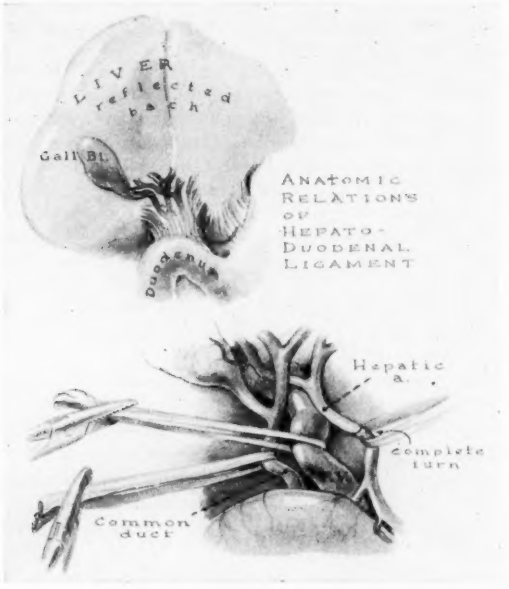

Fig. 2.—Illustrations showing how structures in hepatoduodenal ligament were teased apart and individually looped with small sized Penrose drains. Double loop was placed around hepatic artery. In this way, it was felt, all blood going into liver could be controlled. Backflow from hepatic radicals of inferior vena cava might still need to be stemmed by direct pressure or mass suturing. In this case there was but little bleeding from raw surface of liver substance, which had been teased apart, except for the capsule, which had been incised with a knife. Structures were not actually dissected out as extensively inferiorly or superiorly as shown in lower figure for illustrative purposes.

The right and left hepatic ducts, arteries, and right and left branches of the portal vein were exposed and individually isolated by gently teasing away the surrounding structures. Penrose drains were then separately placed around the common bile duct, the portal vein, and the hepatic artery. The drain controlling the hepatic artery was wrapped around the vessel a full turn, thus creating a cinch-like valve. Traction on this drain should control any accidental hemorrhage from the hepatic artery or its branches. Pulsation above the cinch valve was felt for and found to be present several times during the procedure. The left hepatic triad structures were then each doubly ligated with 00 nonabsorbable surgical (black silk) suture material and transected. After this, the falciform ligament, including the ligamentum teres, was transected, permitting dissection of the left triangular ligament and liberation of the lobe. The greatest difficulty was encountered in the region of the inferior vena cava due to the presence of adjacent dense fibrosis. During this part of the procedure the cyst cavity was entered, with the loss of several small daughter cysts and whitish opalescent fluid. These fell upon previously placed tapes and were thereby completely removed. The defect was treated with 2% formalin and clamped and covered. The lobe was then excised with ease through a narrow isthmus. Bleeding was minimal. Two layers of interlocking continuous 00 chromic absorable surgical (gut) sutures were inserted, incorporating the remaining portion of the falciform ligament for reperitonealization. The wound was closed in layers without drainage, with a total operating time of 2 hours and 55 minutes.

Pathology Report (Dr. S. Koletsky, Western Reserve University).—Gross: "The cut surface consists of multilocular cysts, some of which are gelatinous, with others containing milky white fluid."

Microscopic: "The cyst wall is composed of hyaline fibrous tissue the inner portion of which shows fibroblastic proliferation and a widespread lymphocytic exudate. Along the inner surface several scolices are identified."

Postoperative Course.—The postoperative convalescence was disturbed by a probable right subphrenic cellulitis, which responded readily to antibiotic therapy.

Comment.—This case illustrates the ease of left lobectomy in isolated lesions if proper hemostasis is initially obtained.

SUMMARY

A case of alveolar (multilocular) type of echinococcus cyst of the left lobe of the liver is presented.

A new method of controlling hemorrhage during surgical removal of the left lobe of the liver is described.

Case Reports

CHOLEDOCHODUODENAL FISTULA SECONDARY TO DUODENAL ULCER

COMMANDER J. L. YON (MC), U.S.N.
AND
CAPTAIN L. G. BELL (MC), U.S.N.

INTERNAL biliary fistulas, although not common, are no longer surgical curiosities. Choledochoduodenal fistulas, other than those secondary to cholelithiasis, are, however, extremely rare. Judd and Burden,[1] in their review of 153 cases of internal biliary fistula at the Mayo Clinic in which surgery had been performed, found only 1 such fistula between the common duct and the duodenum, while they encountered 148 between the gall bladder and the duodenum. They felt that all of these fistulas had been caused by cholelithiasis. Davison and Aries[2] found only 7 cases of internal biliary fistula in 6,000 autopsies at Cook County Hospital, and in none of these was an antemortem diagnosis made. Bernard,[3] according to Eliason and Stevens,[4] found 109 such fistulas in 6,263 patients having surgical intervention upon the biliary system, an incidence of 1.8% in biliary tract surgery. Those authors describe the following types of biliary fistulas: (1) communication between the biliary tree and the esophagus, stomach, duodenum, jejunum, ileum, appendix, or colon; (2) communication between the biliary tree and the bronchi or the pleura, and (3) fistulas between the biliary tree and the urinary tract, umbilicus, Fallopian tubes, uterus, vagina, ovarian cysts, or pericardium. The biliary tree is understood to include the liver, gall bladder, and extrahepatic ducts. The gall bladder is by far the most commonly involved portion of the biliary tree. Eliason and Stevens also state that the primary cause of such fistulas, with the exception of the isolated case, is a complication of one of the following preexisting diseases: (*a*) chronic calculous cholecystitis, (*b*) peptic ulcer, or (*c*) malignant growth in the gastrointestinal tract. Well over 90% are due to chronic cholecystitis with cholelithiasis. The high incidence in females in the ratio of 3:1 over males is merely a reflection of the usual preponderance of gall-bladder disease in women.

Internal biliary fistulas are seldom diagnosed preoperatively unless they are visualized by the roentgenologist during gastrointestinal contrast studies. Wein-

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1. Judd, E. S., and Burden, V. G.: Internal Biliary Fistula, Ann. Surg. **81**:305-312 (Jan.) 1925.

2. Davison, M., and Aries, L. J.: Spontaneous Choledochogastrostomy and Cholecystogastrostomy, Ann. Surg. **107**:229-237 (Feb.) 1938.

3. Bernard, F.: Spontaneous Internal Fistulae: Operative Treatment, Deutsche Ztschr. Chir. **242**:493-506; 736-756, 1934.

4. Eliason, E. L., and Stevens, L. W.: Spontaneous Internal Biliary Fistula, Am. J. Surg. **51**:387-392 (Feb.) 1941.

berger and Rosenthal[5] have stated that retrograde filling of the biliary tree by barium during the course of a routine gastrointestinal x-ray may be caused by (1) penetrating gallstones from the gall bladder, or, very much less frequently, from the common duct into the duodenum, leaving a fistula; (2) extension of an inflammatory process by contiguity from the gall bladder or the common duct to the duodenum and vice versa; (3) the establishment of a fistula by the extension by contiguity of a primary inflammatory lesion of the colon; (4) operative intervention resulting in cholecystoduodenostomy, cholecystogastrostomy or cholecystojejunostomy, and (5) questionable physiological reflux from the duodenum through a patent sphincter of Oddi into the biliary tree. They report the case of an Army inductee who gave an ulcer history of six years' duration. Roentgenograms revealed a choledochoduodenal fistula. It was assumed that the cause of this lesion was an ulcer eroding into the common duct because an oral cholecystogram had failed to reveal calculi. This person was disqualified for the service and advised to see his local physician. It is not known whether the x-ray impression was confirmed by surgery.

REPORT OF A CASE

The following case, somewhat similar to that of Weinberger and Rosenthal, was confirmed by surgery.

C. S., a 57-year-old Negro man, was admitted to the hospital complaining of intermittent paraumbilical pain for the six months preceding his admission. The pain was sharp and nonradiating in character and was relieved by food and alkalies. His symptoms had become more frequent, being principally nocturnal in occurrence, until their severity caused him to seek treatment in the hospital for relief. In addition to his primary complaint he had a history of nocturia (four or five times), with increasing difficulty in starting urination. There had been no weight loss, jaundice, nausea, vomiting, or change in bowel habits, or bloody or tarry stools.

The past surgical history revealed an appendectomy in 1937, for a perforated appendix. A lysis of adhesions in the cecal region was performed in 1940, for the relief of intestinal obstruction.

The positive physical findings were as follows: blood pressure 170/100 and moderate cardiac enlargement with Grade I arteriosclerotic changes of the retinal vessels. Abdominal palpation revealed generalized tenderness, localized in the epigastrium, with no muscle rigidity, rebound pain, or masses. There were no abnormal bowel sounds.

Laboratory studies gave the following findings: red blood cell count 4,700,000; hemoglobin, 13 gm. per 100 cc., and white blood cell count 5,100, with 54 neutrophiles, 45 lymphocytes, and 1 eosinophile. The urine was slightly cloudy and acid, with a specific gravity of 1.005 and a negative reaction for albumin. The urine culture yielded hemolytic Staphylococcus albus. The Kahn reaction was negative, and prothrombin was 100%. Reactions to the thymol turbidity and cephalin flocculation tests were within normal limits. The urine was found to concentrate to 1.018 on repeated analysis. A urologic consultant reported mild bladder-neck obstruction, but surgery was not recommended. Electrocardiographic findings were consistent with moderate myocardial damage. A chest x-ray disclosed that the heart was enlarged to the left, with no pathology of the lungs or great vessels. Gastrointestinal contrast studies showed that the esophagus and stomach were normal. The stomach emptied well with active peristalsis. The duodenal cap was small with a persistent deformity. The barium outlined a tract which appeared to lead from the deformed duodenal cap (Fig. 1) upward for about 7 cm. It was felt that this most likely represented a fistula leading from the deformed duodenal cap to the liver. An active ulcer was also seen on the medial aspect of the deformed cap opposite this tract. In the five-hour film

5. Weinberger, J., and Rosenthal, A.: Choledochoduodenal Fistula: Case Report, Am. J. Roentgenol, **53**:470-473 (May) 1945.

there was a retained fleck of barium in the ulcer crater. The gall bladder failed to visualize on the cholecystogram, and there was no evidence of radiopaque calculi. The barium enema revealed nothing abnormal.

It was believed that this patient had a choledochoduodenal fistula, probably due to an old ulcer, with another active ulcer of the duodenum. Subtotal gastrectomy was advised. When the abdominal cavity was opened the stomach, the transverse colon, and a loop of small bowel were adherent to the anterior abdominal wall in the area of the previous scar by firm fibrous adhesions. These were separated, as were some fine adhesions between the duodenum and the under surface of the liver. The anterior-superior surface of the first part of the duodenum was scarred and

Fig. 1.—Preoperative roentgenographic visualization of fistula tract.

fibrotic. The greater curvature of the stomach was mobilized, and there an active ulcer was found on the posterior-inferior surface of the first part of the duodenum. This ulcer was penetrating into the pancreas. By sharp dissection the duodenum was freed from the pancreas and was transected just distal to the pylorus without clamping in order to permit inspection of the interior of the duodenum prior to closing the stump. There was seen immediately an open stoma through which bile was flowing in the scarred anterior-superior duodenal surface just at the edge of the transected duodenum. A probe inserted into the stoma and through the fistulous tract passed readily into the common duct. The common duct, both proximal and distal to the junction of the tract, was explored, with negative findings. The gall bladder was thin walled and of a normal bluish color, with no evidence of old or recent inflammation, and it contained no

stones. Pressure on the gall bladder caused bile to pour from the fistulous tract. Any attempt at routine closure of the duodenal stump would have obliterated the stoma of this functioning biliary tract. It was also felt that obliteration of this tract might predispose to possible biliary obstruction or to an insecure closure of the duodenal stump or both. The closure was therefore accomplished by dividing the septum between the fistula and the duodenum for approximately 2.5 cm. and approximating the mucosa of the duodenum and the lining of the tract with fine nonabsorbable surgical (silk) sutures. A small catheter was placed in the fistula and down into the duodenum (Fig. 2) and sutured in place. The duodenal stump was closed in a routine manner above the catheter.

A subtotal gastrectomy was completed with an anterocolic anastomosis, and a drain was placed in the right subhepatic space. The patient had an uneventful recovery, except for some

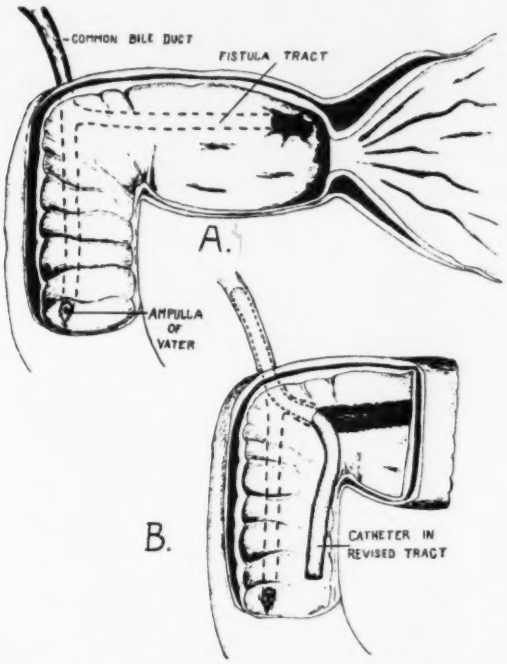

Fig. 2.—*A*, cut-away view of fistula tract entering duodenum. *B*, similar illustration showing reconstructed biliary fistula and closed duodenal stump.

postoperative drainage for five days and rather annoying distention for four days. He subsequently made a rapid recovery and was discharged from the hospital on the 20th postoperative day, with no complaints. He was advised to return for a follow-up but failed to do so. Six months postoperatively he was contacted and returned to the follow-up clinic. He was well nourished, symptom free, eating everything, working steadily, and obviously overindulging in alcoholic beverages. He refused to stay in the hospital for follow-up studies but promised to return in two weeks. He did return in this period in an intoxicated state and, although he was scheduled to have gastrointestinal x-rays, cholecystograms, and gastric analysis, he left the hospital after the gastrointestinal series and refused to return to complete the other studies.

The x-rays and fluoroscopic studies that were completed revealed a small residual gastric pouch with a well-functioning stoma. The afferent jejunal loop contained only a small amount of barium, and the fistulous tract was not visualized.

SUMMARY

A brief review of the literature on biliary intestinal fistulas has been presented. This type of fistula without calculi and associated gall-bladder disease is a rarity. A case report has been presented of a patient with proved choledochoduodenal fistula, in which there was no evidence at surgery of primary disease of the biliary tract or of biliary calculi. The patient reported on did have an active ulcer of the duodenum and evidence of old ulceration. We feel that this is a true choledochoduodenal fistula secondary to a perforating duodenal ulcer. The technical details of a plastic revision of the fistulous opening in the duodenum, utilized to permit closure of the duodenal stump and to assure adequate drainage of the biliary system, have been outlined.

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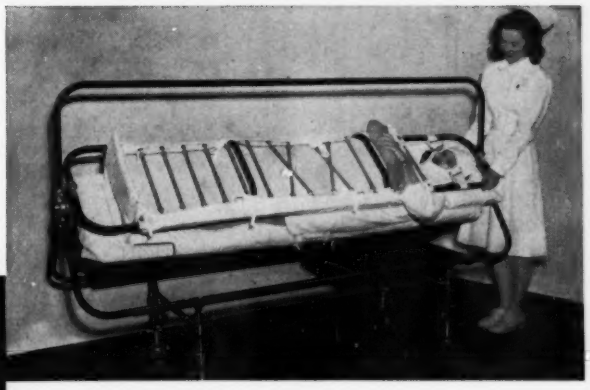

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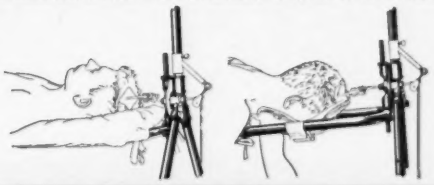

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